WEST Search History

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DATE: Wednesday, May 31, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ	
☐	L51	L50 not @ay>2002	242
☐	L50	L49 and polymer	342
☐	L49	L48 and L11	375
☐	L48	L45 and L3	520
☐	L47	L45 and L1	3
☐	L46	L45 an dl1	0
☐	L45	L44 or L43 or L42	43146
☐	L44	(424/484 |424/486 |424/489 |424/490 |424/491)![CCLS]	7810
☐	L43	(514/962 |514/963)![CCLS]	773
☐	L42	(435/6)![CCLS]	34779
☐	L41	L40 and L9	18
☐	L40	L36 not L39	18
☐	L39	L36 not L37	112
☐	L38	L37 not L36	337
☐	L37	L29 or L28	355
☐	L36	L35 not @ay>2001	130
☐	L35	L34 and L9	390
☐	L34	L33 and L11	478
☐	L33	L32 and L2	676
☐	L32	L31 and L7	716
☐	L31	L30 or L29 or L28	1570
☐	L30	L27.clm.	1396
☐	L29	L27.ab.	337
☐	L28	L27.ti.	163
☐	L27	L26 or L19	11051
☐	L26	interleukin NEAR2 12	3542
☐	L25	L24 not @ay>2002	16
☐	L24	L23 and L9	34
☐	L23	L22 and L2	37
☐	L22	L21 and L11	40
☐	L21	L20 and L7	58

☐	L20	L19.ab.	258
☐	L19	IL NEAR2 12	9726
☐	L18	L17 not @py>2001	8
☐	L17	L16 and L9	54
☐	L16	L7 and L15	64
☐	L15	L14 and L3	113
☐	L14	L11.ab.	33131
☐	L13	L3 and L6	3453
☐	L12	L10 and L11	2
☐	L11	liposom$ or microspher$ or encapsula$	265751
☐	L10	L8 and L9	5
☐	L9	oral$	207750
☐	L8	L7 and L5	5
☐	L7	gastrointestin$ or esophag$ or gastic? or intestin$ or colorectal$	123970
☐	L6	gastrointestin$ or esophag$ or gastic? or intestin? or colorectal?	92112
☐	L5	L2 and L4	8
☐	L4	L3.ab.	25
☐	L3	sulindac	5294
☐	L2	cancer$ or tumor$ or neoplas$	190275
☐	L1	egilmez.in.	7

END OF SEARCH HISTORY

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NEWS 4 OCT 03 MATHDI removed from STN
NEWS 5 OCT 04 CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 6 OCT 13 New CAS Information Use Policies Effective October 17, 2005
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FILE 'HOME' ENTERED AT 09:22:46 ON 14 DEC 2005

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

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* available and contains the CA role and document type information. *
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http://www.cas.org/ONLINE/UG/regprops.html

```
=> E "SULINDAC"/CN 25
E1          1    SULIKOL K/CN
E2          1    SULIN/CN
E3          1 --> SULINDAC/CN
E4          1    SULINDAC B .OMEGA.-N-METHYL-L-ARGININE SALT/CN
E5          1    SULINDAC B .OMEGA.-N-NITRO-L-ARGININE METHYL ESTER SALT/
E6          1    SULINDAC B .OMEGA.-N-NITRO-L-ARGININE SALT/CN
E7          1    SULINDAC ETHYL ESTER/CN
E8          1    SULINDAC SODIUM/CN
E9          1    SULINDAC SULFIDE/CN
E10         1    SULINDAC SULFONE/CN
E11         1    SULINDAC SULFOXIDE/CN
E12         1    SULINDAC-QUINOLINE/CN
E13         1    SULINEX/CN
E14         1    SULINOL/CN
E15         1    SULIODOVIZOL/CN
E16         1    SULISATIN/CN
E17         1    SULISATIN DISODIUM SALT/CN
E18         1    SULISATIN SODIUM/CN
E19         1    SULISATINE SODIUM/CN
E20         1    SULISOBENZONE/CN
E21         1    SULJEX/CN
E22         1    SULKA/CN
E23         1    SULKA K BOLUSES/CN
E24         1    SULKA N/CN
E25         1    SULKOR/CN

=> S E3
L1          1 SULINDAC/CN

=> file caplus
COST IN U.S. DOLLARS                    SINCE FILE     TOTAL
                                  ENTRY   SESSION
FULL ESTIMATED COST                        5.03      5.24

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FILE COVERS 1907 - 14 Dec 2005 VOL 143 ISS 25
FILE LAST UPDATED: 13 Dec 2005 (20051213/ED)


```
=> s l1
L2       1426 L1

=> s gastrointestingal or esophag? or gastic? or intestin? or colorect?
            2 GASTROINTESTINGAL
        15568 ESOPHAG?
            4 GASTIC?
       239459 INTESTIN?
        18675 COLORECT?
L3      254068 GASTROINTESTINGAL OR ESOPHAG? OR GASTIC? OR INTESTIN?
               T?

=> s cancer? or tumor? or neoplas? or polyp?
       277857 CANCER?
       411659 TUMOR?
       431921 NEOPLAS?
       438716 POLYP?
L4     1099978 CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?

=> s l4 and l3
L5       65506 L4 AND L3

=> s l5 and l2
L6         234 L5 AND L2

=> s oral?
L7       243958 ORAL?

=> s l7 and l6
L8          30 L7 AND L6

=> s l2 (l) l4
L9         186 L2 (L) L4

=> s l9 and l3
L10        121 L9 AND L3

=> s l10 and l7
L11         14 L10 AND L7

=> s l14 not py>2002
L14 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l11 not py>2002
      3346380 PY>2002
L12          9 L11 NOT PY>2002

=> d ibib 1-4

L12  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2002:723268  CAPLUS
DOCUMENT NUMBER:         138:13001
TITLE:                     A mouse model of human   ***oral***  -
                         ***esophageal***   cancer
AUTHOR(S):                    Opitz, Oliver G.; Harada, Hideki; Suliman, Yasir;
                         Rhoades, Ben; Sharpless, Norman E.; Kent, Ralph;
                         Kopelovich, Levy; Nakagawa, Hiroshi; Rustgi, Anil K.
CORPORATE SOURCE:        Division of Gastroenterology, University of
                         Pennsylvania, Philadelphia, PA, 19104-2144, USA
```

SOURCE: Journal of Clinical Investigation (2002), 110(6), 761-769
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:259707 CAPLUS
DOCUMENT NUMBER: 136:379639
TITLE: Primary chemoprevention of familial adenomatous polyposis with sulindac
AUTHOR(S): Giardiello, Francis M.; Yang, Vincent W.; Hylind, Linda M.; Krush, Anne J.; Petersen, Gloria M.; Trimbath, Jill D.; Piantadosi, Steven; Garrett, Elizabeth; Geiman, Deborah E.; Hubbard, Walter; Offerhaus, Johan A.; Hamilton, Stanley R.
CORPORATE SOURCE: Dep. Med., Johns Hopkins Univ. Sch. Med., Baltimore, MD, USA
SOURCE: New England Journal of Medicine (2002), 346(14), 1054-1059
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:564792 CAPLUS
DOCUMENT NUMBER: 135:127230
TITLE: Method for inhibiting a tumor
INVENTOR(S): Nair, Muraleedharan G.; Bourquin, Leslie D.; Seeram, Navindra P.; Kang, Soo-Young
PATENT ASSIGNEE(S): Michigan State University, USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054516	A1	20010802	WO 2001-US1196	20010112

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2398389	AA	20010802	CA 2001-2398389	20010112

PRIORITY APPLN. INFO.: US 2000-494077 A 20000128
WO 2001-US1196 W 20010112
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FC RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:476884 CAPLUS
DOCUMENT NUMBER: 135:282815
TITLE: Sulindac in familial adenomatous polyposis: Evaluation by nuclear morphometry
AUTHOR(S): Fernandez-Lopez, F.; Conde-Freire, R.; Cadarso-Suarez, C.; Garcia-Iglesias, J.; Puente-Dominguez, J. L.; Potel-Lesquereux, J.
CORPORATE SOURCE: General Surgery Department, Hospital Clinico Universitario, Santiago de Compostela, Spain
SOURCE: European Journal of Surgery (2001), 167(5), 375-381
CODEN: EUJSEH; ISSN: 1102-4151

PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib 5-9

L12 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:260877 CAPLUS
DOCUMENT NUMBER: 133:217169
TITLE: Sulindac and acetylsalicylic acid (ASA) - clinical relevance in familial adenomatous polyposis
AUTHOR(S): Winde, G.
CORPORATE SOURCE: Klinik und Poliklinik fur Allgemeine Chirurgie der WWU, Munster, D-48129, Germany
SOURCE: Falk Symposium (1999), 109(Colorectal Cancer), 235-255
CODEN: FASYDI; ISSN: 0161-5580
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:147314 CAPLUS
DOCUMENT NUMBER: 132:273995
TITLE: Inhibition of rat colon tumors by sulindac and sulindac sulfone is independent of K-ras (codon 12) mutation
AUTHOR(S): De Jong, Tanya A.; Skinner, Stewart A.; Malcontenti-Wilson, Cathy; Vogiagis, Daphne; Bailey, Michael; Van Driel, Ian R.; O'Brien, Paul E.
CORPORATE SOURCE: Department of Surgery, Monash University Medical School, Melbourne, 3181, Australia
SOURCE: American Journal of Physiology (2000), 278(2, Pt. 1), G266-G272
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:18902 CAPLUS
DOCUMENT NUMBER: 132:44655
TITLE: Rectal epithelial apoptosis in familial adenomatous polyposis patients treated with sulindac
AUTHOR(S): Keller, J. J.; Offerhaus, G. J. A.; Polak, M.; Goodman, S. N.; Zahurak, M. L.; Hylind, L. M.; Hamilton, S. R.; Giardiello, F. M.
CORPORATE SOURCE: Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Gut (1999), 45(6), 822-828
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:277228 CAPLUS
DOCUMENT NUMBER: 124:331957
TITLE: Sulindac induced regression of ***colorectal*** adenomas in familial adenomatous polyposis: Evaluation of predictive factors
AUTHOR(S): Giardiello, F. M.; Offerhaus, J. A.; Tersmette, A. C.; Hylind, L. M.; Krush, A. J.; Brensinger, J. D.; Booker, S. V.; Hamilton, S. R.
CORPORATE SOURCE: School Medicine, Johns Hopkins University, Baltimore, MD, 21287, USA

SOURCE: Gut (1996), 38(4), 578-581
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:529697 CAPLUS
DOCUMENT NUMBER: 115:129697
TITLE: Lung tumorigenicity of NNK given ***orally*** to A/J mice: its application to chemopreventive efficacy studies
AUTHOR(S): Castonguay, Andre; Pepin, Pierrot; Stoner, Gary D.
CORPORATE SOURCE: Sch. Pharm., Laval Univ., Quebec, QC, G1K 7P4, Can.
SOURCE: Experimental Lung Research (1991), 17(2), 485-99
CODEN: EXLRDA; ISSN: 0190-2148
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d abs 9

L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AB The ability of five chemopreventive agents to inhibit 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced lung tumors in A/J mice was detd. The carcinogen was administered in the drinking water during 7 wk (at doses of 9.2 to 3.1 mg/mouse). Three chemopreventive agents: (dose, g/kg diet) ellagic acid (4.0), 2(3)-BHA (5.0), and sulindac (0.13) inhibited the multiplicity of lung adenomas by 52, 88, and 52%, resp., when compared to NNK controls. .beta.-Carotene + retinol (2.14 + 0.009), in combination, and selenium (0.0022) were ineffective. NNK was absorbed more rapidly from the duodenum than from the stomach and was metabolized in both tissues. The activation of NNK by .alpha.-carbon hydroxylation and its deactivation by pyridine N-oxidn. was more extensive in the duodenum than in the stomach. Carbonyl redn. of NNK was 10 times higher in the duodenum. Liver microsomes were more active than lung microsomes in the .alpha.-carbon hydroxylation of NNK, suggesting that some liver isoenzymes of cytochrome P 450 have a high affinity for NNK. Pyridine N-oxidn. was five times more extensive in lung microsomes than in liver microsomes. Collectively, these results demonstrate that NNK given ***orally*** to A/J mice provides a suitable model from which to assess the relative activity and mechanisms of action of chemopreventive agents in pulmonary carcinogenesis.

=> d kwic 9

L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
TI Lung tumorigenicity of NNK given ***orally*** to A/J mice: its application to chemopreventive efficacy studies
AB . . . N-oxidn. was five times more extensive in lung microsomes than in liver microsomes. Collectively, these results demonstrate that NNK given ***orally*** to A/J mice provides a suitable model from which to assess the relative activity and mechanisms of action of chemopreventive. . .
IT ***Intestine*** , metabolism
(duodenum, (methylnitrosamino)(pyridyl)butanone metab. by, chemopreventive agents agents against lung neoplasm effect on)
IT 68-26-8, Retinol 476-66-4, Ellagic acid 7235-40-7, .beta.-Carotene 14124-67-5, Selenite 25013-16-5 ***38194-50-2*** , Sulindac
RL: BIOL (Biological study)
((methylnitrosamino)(pyridyl)butanone-induced lung ***neoplasm*** response to)

=> d ibib abs keic 8
'KEIC' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers

CBIB -------- AN, plus Compressed Bibliographic Data
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DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
containing hit terms
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HITSTR ------ HIT RN, its text modification, its CA index name, and
its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
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OCC --------- Number of occurrence of hit term and field in which it occurs

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to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> d ibib abs kwic 8

L12 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:277228 CAPLUS
DOCUMENT NUMBER: 124:331957
TITLE: Sulindac induced regression of ***colorectal***
adenomas in familial adenomatous polyposis: Evaluation
of predictive factors
AUTHOR(S): Giardiello, F. M.; Offerhaus, J. A.; Tersmette, A. C.;
Hylind, L. M.; Krush, A. J.; Brensinger, J. D.;
Booker, S. V.; Hamilton, S. R.
CORPORATE SOURCE: School Medicine, Johns Hopkins University, Baltimore,
MD, 21287, USA
SOURCE: Gut (1996), 38(4), 578-581
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background-Sulindac, a non-steroidal anti-inflammatory drug, causes
regression of ***colorectal*** adenomas in patients with familial

adenomatous polyposis (FAP) but the response is variable. Specific clin. factors predictive of sulindac induced regression have not been studied. Methods-22 patients with FAP were given sulindac 150 mg ***orally*** twice a day. Polyp no. and size were detd. before treatment and at three months. The relation of nine clin. factors to polyp regression (per cent of baseline polyp no. after treatment) was evaluated by univariate and multivariate anal. Results-After three months of sulindac, polyp no. had decreased to 45 per cent of baseline and polyp size to 50 per cent of baseline ($p<0.001$ and $p<0.01$, resp.). Univariate anal. showed greater polyp regression in older patients ($p=0.004$), those with previous colectomy and ileorectal anastomosis ($p=0.001$), and patients without identifiable mutation of the APC gene responsible for FAP ($p=0.05$). With multivariate regression anal., response to sulindac treatment was assocd. with previous subtotal colectomy. Conclusions-Sulindac treatment seems effective in producing regression of ***colorectal*** adenomas of FAP patients with previous subtotal colectomy regardless of baseline polyp no. and size. Changed sulindac metab., reduced area of the target mucosa, or changed epithelial characteristics after ileorectal anastomosis may explain these findings.

TI Sulindac induced regression of ***colorectal*** adenomas in familial adenomatous polyposis: Evaluation of predictive factors

AB Background-Sulindac, a non-steroidal anti-inflammatory drug, causes regression of ***colorectal*** adenomas in patients with familial adenomatous polyposis (FAP) but the response is variable. Specific clin. factors predictive of sulindac induced regression have not been studied. Methods-22 patients with FAP were given sulindac 150 mg ***orally*** twice a day. Polyp no. and size were detd. before treatment and at three months. The relation of nine clin. factors to polyp regression (per cent of baseline polyp no. after treatment) was evaluated by univariate and multivariate anal. Results-After three months of sulindac, polyp no. had decreased to 45 per cent of baseline and polyp size to 50 per cent of baseline ($p<0.001$ and $p<0.01$, resp.). Univariate anal. showed greater polyp regression in older patients ($p=0.004$), those with previous colectomy and ileorectal anastomosis ($p=0.001$), and patients without identifiable mutation of the APC gene responsible for FAP ($p=0.05$). With multivariate regression anal., response to sulindac treatment was assocd. with previous subtotal colectomy. Conclusions-Sulindac treatment seems effective in producing regression of ***colorectal*** adenomas of FAP patients with previous subtotal colectomy regardless of baseline polyp no. and size. Changed sulindac metab., reduced area of the target mucosa, or changed epithelial characteristics after ileorectal anastomosis may explain these findings.

ST sulindac ***colorectal*** adenomas adenomatous polyposis

IT Neoplasm inhibitors
(large ***intestine*** , sulindac induced regression of ***colorectal*** adenomas in familial adenomatous polyposis in humans)

IT ***Intestine*** , neoplasm
(large, inhibitors, sulindac induced regression of ***colorectal*** adenomas in familial adenomatous polyposis in humans)

IT ***38194-50-2*** , Sulindac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulindac induced regression of ***colorectal*** adenomas in familial adenomatous ***polyposis*** in humans)

=> d ibib abs kwic 2

L12 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:259707 CAPLUS
DOCUMENT NUMBER: 136:379639
TITLE: Primary chemoprevention of familial adenomatous polyposis with sulindac
AUTHOR(S): Giardiello, Francis M.; Yang, Vincent W.; Hylind, Linda M.; Krush, Anne J.; Petersen, Gloria M.; Trimbath, Jill D.; Piantadosi, Steven; Garrett, Elizabeth; Geiman, Deborah E.; Hubbard, Walter; Offerhaus, Johan A.; Hamilton, Stanley R.
CORPORATE SOURCE: Dep. Med., Johns Hopkins Univ. Sch. Med., Baltimore, MD, USA
SOURCE: New England Journal of Medicine (2002), 346(14), 1054-1059

CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Familial adenomatous polyposis is caused by a germ-line mutation in the adenomatous polyposis coli gene and is characterized by the development of hundreds of ***colorectal*** adenomas and, eventually, ***colorectal*** cancer. Nonsteroidal antiinflammatory drugs can cause regression of adenomas, but whether they can prevent adenomas is unknown. Methods: The authors conducted a randomized, double-blind, placebo-controlled study of 41 young subjects (age range, 8 to 25 yr) who were genotypically affected with familial adenomatous polyposis but phenotypically unaffected. The subjects received either 75 or 150 mg of sulindac ***orally*** twice a day or identical-appearing placebo tablets for 48 mo. The no. and size of new adenomas and side effects of therapy were evaluated every four months for four years, and the levels of five major prostaglandins were serially measured in biopsy specimens of normal-appearing ***colorectal*** mucosa. Results: After four years of treatment, the av. rate of compliance exceeded 76 % in the sulindac group, and mucosal prostaglandin levels were lower in this group than in the placebo group. During the course of the study, adenomas developed in 9 of 21 subjects (43 %) in the sulindac group and 11 of 20 subjects in the placebo group (55 %) (P = 0.54). There were no significant differences in the mean no. (P = 0.69) or size (P = 0.17) of polyps between the groups. Sulindac did not slow the development of adenomas, according to an evaluation involving linear longitudinal methods. Conclusions: Std. doses of sulindac did not prevent the development of adenomas in subjects with familial adenomatous polyposis.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Background: Familial adenomatous polyposis is caused by a germ-line mutation in the adenomatous polyposis coli gene and is characterized by the development of hundreds of ***colorectal*** adenomas and, eventually, ***colorectal*** cancer. Nonsteroidal antiinflammatory drugs can cause regression of adenomas, but whether they can prevent adenomas is unknown. Methods: The authors conducted a randomized, double-blind, placebo-controlled study of 41 young subjects (age range, 8 to 25 yr) who were genotypically affected with familial adenomatous polyposis but phenotypically unaffected. The subjects received either 75 or 150 mg of sulindac ***orally*** twice a day or identical-appearing placebo tablets for 48 mo. The no. and size of new adenomas and side effects of therapy were evaluated every four months for four years, and the levels of five major prostaglandins were serially measured in biopsy specimens of normal-appearing ***colorectal*** mucosa. Results: After four years of treatment, the av. rate of compliance exceeded 76 % in the sulindac group, and mucosal prostaglandin levels were lower in this group than in the placebo group. During the course of the study, adenomas developed in 9 of 21 subjects (43 %) in the sulindac group and 11 of 20 subjects in the placebo group (55 %) (P = 0.54). There were no significant differences in the mean no. (P = 0.69) or size (P = 0.17) of polyps between the groups. Sulindac did not slow the development of adenomas, according to an evaluation involving linear longitudinal methods. Conclusions: Std. doses of sulindac did not prevent the development of adenomas in subjects with familial adenomatous polyposis.
IT Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***colorectal*** mucosa prostaglandin levels as measure of sulindac local effect in humans with familial adenomatous polyposis)
IT Antitumor agents
(***colorectal*** , adenoma; primary chemoprevention of familial adenomatous polyposis with sulindac in humans)
IT ***Intestine*** , neoplasm
(***colorectal*** , inhibitors, adenoma; primary chemoprevention of familial adenomatous polyposis with sulindac in humans)
IT ***Intestine*** , neoplasm
(familial polyposis; primary chemoprevention of familial adenomatous polyposis with sulindac in humans)
IT ***Intestine***
(large, mucosa; ***colorectal*** mucosa prostaglandin levels as measure of sulindac local effect in humans with familial adenomatous polyposis)
IT 363-24-6, Prostaglandin E2 551-11-1, Prostaglandin F2.alpha.
13367-85-6, Prostaglandin B2 41598-07-6, Prostaglandin D2 58962-34-8,
6-keto-Prostaglandin F1.alpha.

```
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
      ( ***colorectal***  mucosa prostaglandin levels as measure of
      sulindac local effect in humans with familial adenomatous polyposis)
IT    ***38194-50-2***  , Sulindac
    RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
    activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
      (primary chemoprevention of familial adenomatous  ***polyposis***
      with sulindac in humans)


=> d his

    (FILE 'HOME' ENTERED AT 09:22:46 ON 14 DEC 2005)

    FILE 'REGISTRY' ENTERED AT 09:22:55 ON 14 DEC 2005
            E "SULINDAC"/CN 25
L1           1 S E3

    FILE 'CAPLUS' ENTERED AT 09:23:34 ON 14 DEC 2005
L2        1426 S L1
L3      254068 S GASTROINTESTINGAL OR ESOPHAG? OR GASTIC? OR INTESTI
L4     1099978 S CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?
L5       65506 S L4 AND L3
L6         234 S L5 AND L2
L7      243958 S ORAL?
L8          30 S L7 AND L6
L9         186 S L2 (L) L4
L10        121 S L9 AND L3
L11         14 S L10 AND L7
L12          9 S L11 NOT PY>2002

=> s lipsom? or microspher? or encapsulat? or polymer?
          74 LIPSOM?
       27180 MICROSPHER?
       55572 ENCAPSULAT?
     1820552 POLYMER?
       84067 POLYMD
       84067 POLYMD
             (POLYMD)
       31147 POLYMG
      326031 POLYMN
        8505 POLYMNS
      327118 POLYMN
             (POLYMN OR POLYMNS)
     1885881 POLYMER?
             (POLYMER? OR POLYMD OR POLYMG OR POLYMN)
L13    1945587 LIPSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?

=> s l13 and l12
L14          0 L13 AND L12

=> s l4 and l2
L15        443 L4 AND L2

=> s l9 and l13
L16         12 L9 AND L13

=> s l16 not py>2002
     3346380 PY>2002
L17          3 L16 NOT PY>2002

=> d ibib 1-3

L17  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2001:430708  CAPLUS
DOCUMENT NUMBER:         135:236055
TITLE:                   Rat colorectal tumors treated with a range of
                         nonsteroidal anti-inflammatory drugs show altered
                         cyclooxygenase-2 and cyclooxygenase-1 splice variant
                         mRNA expression levels
AUTHOR(S):               Vogiagis, Daphne; Brown, Wendy; Glare, Eric M.;
                         O'Brien, Paul E.
CORPORATE SOURCE:        Department of Surgery, Monash University Medical
                         School, Alfred Hospital, Prahran, 3181, Australia
```

SOURCE: Carcinogenesis (2001), 22(6), 869-874
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:457250 CAPLUS
DOCUMENT NUMBER: 129:76490
TITLE: Method for treating a tumor with a chemotherapeutic agent and nonemulsified ultrapurified ***polymerized*** hemoglobin solution
INVENTOR(S): Teicher, Beverly A.; Rausch, Carl W.; Hopkins, Robert E., II
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA; Biopure Corp.
SOURCE: U.S., 16 pp., Cont.-in-part of U. S. Ser. No. 94,501.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776898	A	19980707	US 1995-477110	19950607
US 5679638	A	19971021	US 1993-94501	19930720

PRIORITY APPLN. INFO.: US 1991-699769 A2 19910514
US 1993-94501 A2 19930720
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:689536 CAPLUS
DOCUMENT NUMBER: 127:326520
TITLE: Method for treating a tumor with a chemotherapeutic agent
INVENTOR(S): Teicher, Beverly A.; Rausch, Carl W.; Hopkins, Robert E., II
PATENT ASSIGNEE(S): Biopure Corporation, USA; Dana Farber Cancer Institute
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 699,769,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5679638	A	19971021	US 1993-94501	19930720
US 5776898	A	19980707	US 1995-477110	19950607

PRIORITY APPLN. INFO.: US 1991-699769 B2 19910514
US 1993-94501 A2 19930720

=> d ibib abs kwic 1

L17 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:430708 CAPLUS
DOCUMENT NUMBER: 135:236055
TITLE: Rat colorectal tumors treated with a range of nonsteroidal anti-inflammatory drugs show altered cyclooxygenase-2 and cyclooxygenase-1 splice variant mRNA expression levels
AUTHOR(S): Vogiagis, Daphne; Brown, Wendy; Glare, Eric M.; O'Brien, Paul E.
CORPORATE SOURCE: Department of Surgery, Monash University Medical School, Alfred Hospital, Prahran, 3181, Australia
SOURCE: Carcinogenesis (2001), 22(6), 869-874
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce tumor mass by increasing tumor cell apoptosis and decreasing cell proliferation. The classically recognized targets for NSAID action are the two isoforms of the cyclooxygenase (COX) gene, which is responsible for prostaglandin prodn. In the rat, the COX-1 gene expresses an alternatively spliced mRNA COX-1 splice variant (SV) which may, at best, code for a truncated COX-1 protein. Previously, it was reported that COX-1SV mRNA is differentially expressed in the ageing stomach. In this study, carcinogen-treated rats were treated for 23 wk with the NSAIDs celecoxib, sulindac or sulindac sulfone, while untreated rats received vehicle alone. The nos. and vols. of tumor per animal were recorded and histol. was performed. The competitive ***polymerase*** chain reaction, was used to det. whether COX gene expression was altered in colorectal tumors and in regions of adjacent and distant macroscopically normal intestine, from vehicle- or NSAID-treated rats. In addn., COX-1 and COX-2 were immunolocalized in the same tumor and normal colonic tissue. Tumors from animals treated with vehicle or celecoxib expressed elevated levels of COX-2 mRNA in comparison with the adjacent normal mucosa. In contrast, tumors from sulindac- and sulindac sulfone-treated rats expressed less COX-2 mRNA than tumors from vehicle-treated rats. The expression of COX-1 mRNA remained unchanged in all tissues examd. However, COX-1SV mRNA contents were elevated in colorectal tumors and reduced after NSAID treatment to the values in normal colonic mucosa. The results indicate that the antineoplastic actions of NSAIDs may be attributed to COX-dependent and/or COX-independent mechanisms of action. The presence and differential expression of COX-1SV mRNA was also demonstrated in colon tumors. COX-1SV mRNA represents 2% of the total COX-1 mRNA expressed and its role in colon cancer remains to be established.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce tumor mass by increasing tumor cell apoptosis and decreasing cell proliferation. The classically recognized targets for NSAID action are the two isoforms of the cyclooxygenase (COX) gene, which is responsible for prostaglandin prodn. In the rat, the COX-1 gene expresses an alternatively spliced mRNA COX-1 splice variant (SV) which may, at best, code for a truncated COX-1 protein. Previously, it was reported that COX-1SV mRNA is differentially expressed in the ageing stomach. In this study, carcinogen-treated rats were treated for 23 wk with the NSAIDs celecoxib, sulindac or sulindac sulfone, while untreated rats received vehicle alone. The nos. and vols. of tumor per animal were recorded and histol. was performed. The competitive ***polymerase*** chain reaction, was used to det. whether COX gene expression was altered in colorectal tumors and in regions of adjacent and distant macroscopically normal intestine, from vehicle- or NSAID-treated rats. In addn., COX-1 and COX-2 were immunolocalized in the same tumor and normal colonic tissue. Tumors from animals treated with vehicle or celecoxib expressed elevated levels of COX-2 mRNA in comparison with the adjacent normal mucosa. In contrast, tumors from sulindac- and sulindac sulfone-treated rats expressed less COX-2 mRNA than tumors from vehicle-treated rats. The expression of COX-1 mRNA remained unchanged in all tissues examd. However, COX-1SV mRNA contents were elevated in colorectal tumors and reduced after NSAID treatment to the values in normal colonic mucosa. The results indicate that the antineoplastic actions of NSAIDs may be attributed to COX-dependent and/or COX-independent mechanisms of action. The presence and differential expression of COX-1SV mRNA was also demonstrated in colon tumors. COX-1SV mRNA represents 2% of the total COX-1 mRNA expressed and its role in colon cancer remains to be established.

IT ***38194-50-2*** , Sulindac 59973-80-7, Sulindac sulfone 169590-42-5, Celecoxib
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(colorectal ***tumors*** treated with nonsteroidal anti-inflammatory drugs show altered cyclooxygenase-2 and cyclooxygenase-1 splice variant mRNA expression)

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	64.77	70.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

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                                                ENTRY    SESSION
CA SUBSCRIBER PRICE                                -3.65     -3.65

FILE 'MEDLINE' ENTERED AT 09:35:28 ON 14 DEC 2005

 FILE LAST UPDATED: 8 DEC 2005 (20051208/UP). FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 will soon be available. For details
 on the 2005 reload, enter HELP RLOAD at an arrow promt (=>).
 See also:

   http://www.nlm.nih.gov/mesh/
   http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
   http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
   http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s SULINDAC/CN
L18         919 SULINDAC/CN

=> s cancer? or tumor? or neoplas? or polyp?
       547932 CANCER?
       758323 TUMOR?
      1455946 NEOPLAS?
       155044 POLYP?
L19    1879233 CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?

=> s gastrointestingal or esophag? or gastic? or intestin? or colorect?
            1 GASTROINTESTINGAL
       101857 ESOPHAG?
           50 GASTIC?
       293936 INTESTIN?
        45036 COLORECT?
L20     428581 GASTROINTESTINGAL OR ESOPHAG? OR GASTIC? OR INTESTIN?
               T?

=> s l19 and l20
L21     125328 L19 AND L20

=> s l21 and l18
L22         175 L21 AND L18

=> s liposom? or microspher? or encapsulat? or polymer?
        30623 LIPOSOM?
        21357 MICROSPHER?
        15072 ENCAPSULAT?
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L23     407843 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?

=> s l23 and l22
L24           8 L23 AND L22

=> s l24 not py>2002
      1733376 PY>2002
L25           6 L24 NOT PY>2002

=> d ibib 1-3

L25  ANSWER 1 OF 6     MEDLINE on STN
ACCESSION NUMBER:   2002696841     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12458338
TITLE:              Effects of long-term administration of sulindac on APC mRNA
                    and apoptosis in colons of rats treated with azoxymethane.
AUTHOR:             Kishimoto Y; Yashima K; Morisawa T; Ohishi T; Marumoto A;
                    Sano A; Idobe-Fujii Y; Miura N; Shiota G; Murawaki Y;
```

Hasegawa J
CORPORATE SOURCE: Division of Pharmacotherapeutics, Department of Pathophysiological and Therapeutic Science, Faculty of Medicine, Tottori University, 86 Nishicho, Yonago 683-8503, Japan.. ykishimo@grape.med.tottori-u.ac.jp
SOURCE: Journal of cancer research and clinical oncology, (2002 Nov) 128 (11) 589-95. Electronic Publication: 2002-10-04. Journal code: 7902060. ISSN: 0171-5216.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030118
Entered Medline: 20030117

L25 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001065648 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11093808
TITLE: Growth-suppressive effect of non-steroidal anti-inflammatory drugs on 11 colon- ***cancer*** cell lines and fluorescence differential display of genes whose expression is influenced by sulindac.
AUTHOR: Akashi H; Han H J; Iizaka M; Nakamura Y
CORPORATE SOURCE: Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, University of Tokyo, Tokyo, Japan.
SOURCE: International journal of cancer. Journal international du cancer, (2000 Dec 15) 88 (6) 873-80. Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222

L25 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001064500 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11076880
TITLE: Sulindac and a cyclooxygenase-2 inhibitor, etodolac, increase APC mRNA in the colon of rats treated with azoxymethane.
AUTHOR: Kishimoto Y; Takata N; Jinnai T; Morisawa T; Shiota G; Kawasaki H; Hasegawa J
CORPORATE SOURCE: Department of Clinical Pharmacology, Faculty of Medicine, Tottori University, 86 Nishicho, Yonago 683-8503, Japan.. ykishimo@grape.med.tottori-u.ac.jp
SOURCE: Gut, (2000 Dec) 47 (6) 812-9. Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222

=> d ibib 4-6

L25 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2000295032 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10833474
TITLE: Par-4, a proapoptotic gene, is regulated by NSAIDs in human colon carcinoma cells.
AUTHOR: Zhang Z; DuBois R N
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine and Cell Biology, Vanderbilt University Medical Center, Veterans Affairs Medical Center, Nashville, Tennessee, USA.

CONTRACT NUMBER: DK47297 (NIDDK)
P30 CA68485 (NCI)
PO CA77839 (NCI)
SOURCE: Gastroenterology, (2000 Jun) 118 (6) 1012-7.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000629
Last Updated on STN: 20021219
Entered Medline: 20000621

L25 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 1999333404 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10403841
TITLE: Redistribution of activated caspase-3 to the nucleus during butyric acid-induced apoptosis.
AUTHOR: Mandal M; Adam L; Kumar R
CORPORATE SOURCE: Cell Growth Regulation Laboratory, University of Texas M.D Anderson Cancer Center, Houston, Texas, 77030, USA.
SOURCE: Biochemical and biophysical research communications, (1999 Jul 14) 260 (3) 775-80.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 20020420
Entered Medline: 19990816

L25 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 96334961 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8707116
TITLE: Sulindac increases the expression of APC mRNA in malignant colonic epithelial cells: an in vitro study.
AUTHOR: Schnitzler M; Dwight T; Robinson B G
CORPORATE SOURCE: Molecular Genetics Unit, Kolling Institute of Medical Research, Royal North Shore Hospital, St Leonards, NSW, Australia.
SOURCE: Gut, (1996 May) 38 (5) 707-13.
Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 19970203
Entered Medline: 19960910

=> d ibib abs kwic 4

L25 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2000295032 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10833474
TITLE: Par-4, a proapoptotic gene, is regulated by NSAIDs in human colon carcinoma cells.
AUTHOR: Zhang Z; DuBois R N
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine and Cell Biology, Vanderbilt University Medical Center, Veterans Affairs Medical Center, Nashville, Tennessee, USA.
CONTRACT NUMBER: DK47297 (NIDDK)
P30 CA68485 (NCI)
PO CA77839 (NCI)
SOURCE: Gastroenterology, (2000 Jun) 118 (6) 1012-7.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000629
Last Updated on STN: 20021219
Entered Medline: 20000621

AB BACKGROUND & AIMS: Many reports indicate that nonsteroidal anti-inflammatory drugs (NSAIDs) have antineoplastic effects, but the precise molecular mechanism(s) responsible are unclear. We evaluated the effect of cyclooxygenase (COX) inhibitors (NSAIDs) on human colon carcinoma cells (HCA-7) and identified several genes that are regulated after treatment with NS-398, a selective COX-2 inhibitor. METHODS: Differential display ***polymerase*** chain reaction cloning techniques were used to identify genes regulated by treatment with NSAIDs and selective COX-2 inhibitors. RESULTS: A prostate apoptosis response 4 (Par-4) gene was up-regulated after NSAID treatment. Par-4 was first isolated from prostate carcinoma cells undergoing apoptosis, and expression of Par-4 sensitized ***cancer*** cells to apoptotic stimuli. Par-4 levels were increased in cells treated with COX inhibitors such as NS-398, nimesulide, SC-58125, and sulindac sulfide. Treatment of HCA-7 cells with these agents also induced apoptotic cell death. CONCLUSIONS: The results suggest that regulation of Par-4 contributes to the proapoptotic effects of high-dose COX inhibitors (NSAIDs) by serving as a downstream mediator leading to initiation of programmed cell death.

AB . . . cells (HCA-7) and identified several genes that are regulated after treatment with NS-398, a selective COX-2 inhibitor. METHODS: Differential display ***polymerase*** chain reaction cloning techniques were used to identify genes regulated by treatment with NSAIDs and selective COX-2 inhibitors. RESULTS: A. . . was up-regulated after NSAID treatment. Par-4 was first isolated from prostate carcinoma cells undergoing apoptosis, and expression of Par-4 sensitized ***cancer*** cells to apoptotic stimuli. Par-4 levels were increased in cells treated with COX inhibitors such as NS-398, nimesulide, SC-58125, and. . .

CT . . . pharmacology
*Apoptosis: DE, drug effects
Apoptosis: GE, genetics
Blotting, Northern
Blotting, Western
Carrier Proteins: AN, analysis
*Carrier Proteins: GE, genetics
*** Colonic Neoplasms***
Cyclooxygenase Inhibitors: PD, pharmacology
DNA Fragmentation
Gene Expression: DE, drug effects
Gene Expression: PH, physiology
Humans
*** Intestinal Mucosa: CH, chemistry***
****Intestinal Mucosa: CY, cytology***
*** Intestinal Mucosa: EN, enzymology***
*Intracellular Signaling Peptides and Proteins
*Nitrobenzenes: PD, pharmacology
Protein Kinase C: ME, metabolism
Pyrazoles: PD, pharmacology
. . . Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
*Sulfonamides: PD, pharmacology
Sulindac: AA, analogs & derivatives
Sulindac: PD, pharmacology
*** Tumor Cells, Cultured***

RN 123653-11-2 (N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide); 162054-19-5 (1-((4-methylsulfonyl)phenyl)-3-trifluoromethyl-5-(4-fluorophenyl)pyrazole); 32004-67-4 (sulindac sulfide); ***38194-50-2*** *** (Sulindac)*** ; 51803-78-2 (nimesulide)

=> d his

(FILE 'HOME' ENTERED AT 09:22:46 ON 14 DEC 2005)

FILE 'REGISTRY' ENTERED AT 09:22:55 ON 14 DEC 2005
E "SULINDAC"/CN 25
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 09:23:34 ON 14 DEC 2005
L2 1426 S L1

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L3     254068 S GASTROINTESTINGAL OR ESOPHAG? OR GASTIC? OR INTESTI
L4    1099978 S CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?
L5      65506 S L4 AND L3
L6        234 S L5 AND L2
L7     243958 S ORAL?
L8         30 S L7 AND L6
L9        186 S L2 (L) L4
L10       121 S L9 AND L3
L11        14 S L10 AND L7
L12         9 S L11 NOT PY>2002
L13   1945587 S LIPSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?
L14         0 S L13 AND L12
L15       443 S L4 AND L2
L16        12 S L9 AND L13
L17         3 S L16 NOT PY>2002

   FILE 'MEDLINE' ENTERED AT 09:35:28 ON 14 DEC 2005
L18       919 S SULINDAC/CN
L19   1879233 S CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?
L20    428581 S GASTROINTESTINGAL OR ESOPHAG? OR GASTIC? OR INTESTI
L21    125328 S L19 AND L20
L22       175 S L21 AND L18
L23    407843 S LIPOSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER
L24         8 S L23 AND L22
L25         6 S L24 NOT PY>2002

=> file caplus
COST IN U.S. DOLLARS                        SINCE FILE     TOTAL
                                              ENTRY   SESSION
FULL ESTIMATED COST                            3.52     73.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE     TOTAL
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FILE LAST UPDATED: 13 Dec 2005  (20051213/ED)

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=> s liposom? or microspher? or encapsulat? or polymer?
      48683 LIPOSOM?
      27180 MICROSPHER?
      55572 ENCAPSULAT?
    1820552 POLYMER?
      84067 POLYMD
      84067 POLYMD
            (POLYMD)
      31147 POLYMG
     326031 POLYMN
       8505 POLYMNS
     327118 POLYMN
            (POLYMN OR POLYMNS)
    1885881 POLYMER?
            (POLYMER? OR POLYMD OR POLYMG OR POLYMN)
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L26    1984458 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?

=> s l9 and l26
L27        15 L9 AND L26

=> s liposom? or microspher? or encapsulat?
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       27180 MICROSPHER?
       55572 ENCAPSULAT?
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=> s l29 not py>2003
     2266400 PY>2003
L31         0 L29 NOT PY>2003

=> d l29 ibib 1-4

L29  ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:591975  CAPLUS
DOCUMENT NUMBER:         143:53482
TITLE:                   Method for inhibiting the growth of gastrointestinal
                         tract tumors
INVENTOR(S):             Egilmez, Nejat K.
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 21 pp.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

    PATENT NO.          KIND   DATE       APPLICATION NO.       DATE
    ---------------     ----   --------   -------------------   --------
    US 2005147689       A1     20050707   US 2003-748003        20031230
    CA 2491338          AA     20050630   CA 2004-2491338       20041223
PRIORITY APPLN. INFO.:                     US 2003-748003     A  20031230

L29  ANSWER 2 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:14227  CAPLUS
DOCUMENT NUMBER:         142:107439
TITLE:                   Cardiolipin synthesis inhibitor for treatment of
                         cardiovascular disorders, and obesity
INVENTOR(S):             Jamil, Haris; Ahmad, Moghis U.; Ahmad, Imran
PATENT ASSIGNEE(S):      Neopharm, Inc., USA
SOURCE:                  PCT Int. Appl., 48 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

    PATENT NO.          KIND   DATE       APPLICATION NO.       DATE
    ---------------     ----   --------   -------------------   --------
    WO 2005000318       A2     20050106   WO 2004-US20104       20040623
    WO 2005000318       A3     20050414
    WO 2005000318       B1     20050526
       W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
          CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
          GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
          LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
          NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
          TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
       RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
          AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
          EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
          SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
          SN, TD, TG
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PRIORITY APPLN. INFO.: US 2003-480669P P 20030623

L29 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:877933 CAPLUS
DOCUMENT NUMBER: 141:365149
TITLE: Anti-PSGL-1 antibodies and scFv fragments for diagnosis, prognosis and therapy of cancer, metastasis, autoimmune disease and inflammation
INVENTOR(S): Levanon, Avigdor; Ben-Levy, Rachel; Plaksin, Daniel; Szanton, Esther; Hagai, Yocheved; Mar-Chaim, Hagit Hoch
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 49 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004208877	A1	20041021	US 2003-611588	20030630

PRIORITY APPLN. INFO.: US 2002-393491P P 20020701

L29 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:856929 CAPLUS
DOCUMENT NUMBER: 141:348831
TITLE: Antibodies specific to epitopes involving cell rolling, metastasis and inflammation for treatment of tumor, restenosis, thrombosis, autoimmune disease and inflammation
INVENTOR(S): Lazarovits, Janette; Nimrod, Abraham; Hoch, Mar-Chaim Hagit; Levanon, Avigdor
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004202665	A1	20041014	US 2003-610843	20030630

PRIORITY APPLN. INFO.: US 2002-393453P P 20020701

=> file pctfull
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 23.21 96.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE 0.00 -3.65

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FILE LAST UPDATED: 13 DEC 2005 <20051213/UP>
MOST RECENT UPDATE WEEK: 200549 <200549/EW>
FILE COVERS 1978 TO DATE

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=> s SULINDAC
L32 2826 SULINDAC

=> s l32/ab

```
L33         9 (SULINDAC/AB)

=> s cancer? or tumor? or neoplas? or polyp?
       73935 CANCER?
       61948 TUMOR?
       21353 NEOPLAS?
      153344 POLYP?
L34     196562 CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?

=> s l34 and l33
L35         7 L34 AND L33

=> s gastrointestingal or esophag? or gastic? or intestin? or colorect?
           4 GASTROINTESTINGAL
       11126 ESOPHAG?
          83 GASTIC?
       38774 INTESTIN?
        8423 COLORECT?
L36     47131 GASTROINTESTINGAL OR ESOPHAG? OR GASTIC? OR INTESTIN?
            T?

=> s gastrointestinal or esophag? or gastic? or intestin? or colorect?
       28847 GASTROINTESTINAL
           9 GASTROINTESTINALS
       28851 GASTROINTESTINAL
             (GASTROINTESTINAL OR GASTROINTESTINALS)
       11126 ESOPHAG?
          83 GASTIC?
       38774 INTESTIN?
        8423 COLORECT?
L37     59284 GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? O
            ?

=> s l37 and l35
L38         7 L37 AND L35

=> s liposom? or microspher? or encapsulat?
       40590 LIPOSOM?
       15203 MICROSPHER?
       61501 ENCAPSULAT?
L39     90511 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT?

=> s l39 and l38
L40         2 L39 AND L38

=> d ibib 1-2

L40   ANSWER 1 OF 2    PCTFULL  COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:      2001035956 PCTFULL  ED 20020820
TITLE (ENGLISH):       USE OF NSAIDs FOR THE TREATMENT OF PANCREATIC
                       ***CANCER***
TITLE (FRENCH):        UTILISATION DES AINS DANS LE TRAITEMENT DU
                       ***CANCER***  DU PANCREAS
INVENTOR(S):           MARSHALL, Mark, Steven;
                       SWEENEY, Christopher, J.;
                       YIP-SCHNEIDER, Michelle, T.;
                       CROWELL, Pamela, L.
PATENT ASSIGNEE(S):    ADVANCED RESEARCH AND TECHNOLOGY INSTITUTI
                       MARSHALL, Mark, Steven;
                       SWEENEY, Christopher, J.;
                       YIP-SCHNEIDER, Michelle, T.;
                       CROWELL, Pamela, L.
DOCUMENT TYPE:         Patent
PATENT INFORMATION:
                       NUMBER          KIND    DATE
                       ---------------------------------
                       WO 2001035956       A1 20010525
DESIGNATED STATES
     W:                AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
                       CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
                       IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
                       MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
                       TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
                       SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
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DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US31410 A 20001115
PRIORITY INFO.: US 1999-60/165,543 19991115

L40 ANSWER 2 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1999049859 PCTFULL ED 20020515
TITLE (ENGLISH): DFMO AND SULINDAC COMBINATION IN ***CANCER*** CHEMOPREVENTION
TITLE (FRENCH): COMBINAISON DE DFMO ET DE SULINDAC DANS LA CHIMIOPREVENTION DU ***CANCER***
INVENTOR(S): GERNER, Eugene, W.;
MEYSKENS, Frank, L., Jr.
PATENT ASSIGNEE(S): THE ARIZONA BOARD OF REGENTS on behalf of THE UNIVERSITY OF ARIZONA;
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA;
GERNER, Eugene, W.;
MEYSKENS, Frank, L., Jr.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9949859	A1	19991007

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-US6693 A 19990326
PRIORITY INFO.: US 1998-60/079,850 19980328

=> d kwic 1

L40 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
TIEN USE OF NSAIDs FOR THE TREATMENT OF PANCREATIC ***CANCER***
TIFR UTILISATION DES AINS DANS LE TRAITEMENT DU ***CANCER*** DU PAI
ABEN The invention provides a method comprising the use of non-steroidal antiinflammatory drugs (NSAIDs), particularly ***sulindac*** or its analogs to treat pancreatic ***cancer*** .

DETD USE OF NSAIDs FOR THE TREATMENT OF PANCREATIC ***CANCER***
Backgrround of the Invention
Cancer of the pancreas ranks 'ust behind lung ***cancer*** , colon ***cancer*** , and breast ***cancer*** as the most common cause of death by ***cancer*** (1). It is more common among men, and men between the ages of 60 and 70 are most at risk.

The cause of pancreatic ***cancer*** is unknown.
. . .
which are not fully understood, usually is 1 0 significant. The average loss is about 25 pounds. Jaundice occurs if the ***cancer*** blocks the common bile duct. The survival rate with pancreatic ***cancer*** is poor.

By the time the malignant ***tumor*** is identified, it often has spread (metastasized) to other parts of the body. The median survival is little more than six.
. .

5 Often the ***tumor*** cannot be removed by surgery, either because it has invaded vital structures that cannot be removed or because it has spread to distant sites. Chemotherapy and radiation therapy can be used on the ***tumor*** ,

although these treatments often are not beneficial.

. . .

Easton, PA (18th ed., 1990) at pages
1115
There is a large amount of literature on the effect of NSAIDs on
cancer ,
particularly colon ***cancer*** . For example, see H. A. Weiss et
al., Scand J.

. . .

in vitro, but that
indomethacin, ketoralac and NS-398, did not. Sulindac has been
investigated in
combination therapy for the treatment of colon ***cancer*** . See, H.
M. Verheul et al.,
Brit- J. Cance , 79, 114 (1999); F. A. Sinicrope et al., Clin.
Cancer Res-, 2, 37
(1996); and M. Mooghen et al., J. Pathol., LI]6, 394 (1988).

C. P. Duffy et al., Eur. J. ***Cancer*** , 34, 1250 (1998), reported
that the
cytotoxicity of certain chemotherapeutic drugs was enhanced when they
were
combined with certain non-steroidal anti-inflammatory agents. The
effects
observed against human lung ***cancer*** cells and human leukemia
cells were highly
specific and not predictable; i.e., some combinations of NSAID and agent
were
effective and some. . .

. . .

a PCT application (WO98/18490) on October 24,
1997, directed to a combination of a substrate for MRP, which can be an
anti-
cancer drug, and a NSAID that increases the potency of the
anti- ***cancer*** drug.

Therefore, a continuing need exists for methods to control
cancers , and to
increase the potency of anti- ***cancer*** drugs with relatively
non-toxic agents.

Summ= of the Invention
In one aspect, the present invention provides a therapeutic method to
treat
pancreatic ***cancer*** , comprising administering to a mammal
afflicted with
pancreatic ***cancer*** an amount of a NSAID, preferably sulindac
((Z) fluoro
methyl-l-[[4-(methylsulfinyl)phenyl] methylene]-IH-Indene acetic acid),
or
an analocr thereof, preferably one that is a COX-2 inhibitor, effective
to inhibit
the viability of pancreatic ***cancer*** cells of said mammal. The
present invention
also provides a method of increasing the susceptibility of human
pancreatic
cancer cells to a chemotherapeutic agent comprising contacting
the cells with an
effective sensitizing amount of a NSAID, preferably sulindac, or said
analog
thereof Thus, the invention provides a therapeutic method for the
treatment of a
human or other mammal afflicted with pancreatic ***cancer*** ,
wherein an effective
amount of an NSAID, preferably sulindac or said analog thereof is
administered
to a subject afflicted with pancreatic ***cancer*** and undergoing
treatment with a
5 chemotherapeutic (antineoplastic) agent.

Preferably, sulindac is administered in conjunction with one or more
chemotherapeutic agents effective against pancreatic ***cancer***
such as gemcitabine
or 5-FU.

A method of evaluating the ability of sulindac to sensitize pancreatic ***cancer*** cells to a chemotherapeutic agent is also provided. The assay method comprises: (a) isolating a first portion of pancreatic ***cancer*** cells ftom a human ***cancer*** patient; (b) measuring their viability; (c) administering sulindac, or said analog thereof, to said patient; (d) isolating a second portion of pancreatic ***cancer*** cells from said patient; (e) measuring the viability of the second portion of pancreatic ***cancer*** cells; and (f) comparing the viability measured in step (e) with the viability measured in step (b); wherein reduced viability in. . . . (b) and (e) are carried out in the presence of the chemotherapeutic agent, as will be the case when the pancreatic ***cancer*** cells are derived from the blood of a mammal afflicted with pancreatic ***cancer*** .

Thus, a ***cancer*** patient about to undergo, or undergoing, treatment for pancreatic ***cancer*** can be rapidly evaluated to see if he/she will benefit from concurrent chemotherapy and administration of sulindac or an analog thereof.

. . .

Description of the FiVures

Figure 1. Photocopy of a representative immunoblot of pancreatic adenocarcinomas and matched normal tissue. Lysates were prepared from ***tumor*** (T) specimens obtained from six patients, three with matched normal (N) tissue (sample numbers correspond to those listed in Table 1). Lysates. . . expresses neither COX- I or COX

Figure 2. Percent COX-2 expression in patient samples. Values of % COX-2 expression for all ***tumor*** samples, shown by solid circles, and non-nal tissue, shown by open circles, from Table I are plotted. Values for mean, median and range are indicated. The % COX-2 expression for the matched pancreatic ***tumor*** /normal tissue sets is shown in the inset (n = I 1). Lines are drawn between the corresponding ***tumor*** values, shown by solid circles, and non-nal values, shown by the open circles. The difference in COX-2 expression between ***tumor*** and non-nal specimens was determined to be statistically significant (P = 0.004).

Figure 3. COX-2 expression in pancreatic ***tumor*** cell lines. A) COX-2 expression in human pancreatic cell lines detected by immunoblot analysis. The K-ras mutation status of each of the. . .

Figure 4. Effect of COX inhibitors on the growth of pancreatic ***tumor*** cell lines. The cell lines BxPC-3, shown by the black bars, and PaCa-2, shown by the hatched bars, were plated in the. . .

Figure 5. Prostaglandin E2 production. A) PGE2 levels in pancreatic ***tumor*** cell lines. Following incubation of exponentially growing cells with 15 gM arachidonic acid in serum-free media for one hour, PGE2 levels. . .

Figure 6 is a graph depicting the effect of a combination of sulindac and gemcitabine on the growth of pancreatic ***tumor*** cell line BxPC.

Figure 7 is a graph depicting the effect of a combination of sulindac and gemcitabine on the growth of pancreatic ***tumor*** cell line PaCa

Detailed Description of the Invention

Difficulty in achieving early diagnosis as well as the aggressive nature of pancreatic ***cancer*** contribute to the low survival rate of patients with pancreatic ***cancer*** . Since few options exist for the treatment of pancreatic ***cancer*** , it is important to identify potential targets for drug therapy. In an effort to gain more insight into pancreatic tumonigenesis] pancreatic ***tumors*** have been analyzed at the molecular level to detect genetic lesions. Activating mutations within the K-ras gene have been detected in up to 90% of pancreatic carcinomas, suggesting that activation of the Ras pathway is important in the development of pancreatic ***cancer*** (2). Experimental chemotherapeutic strategies for pancreatic ***cancer*** patients currently include drugs which target the Ras signal transduction pathway.

. . .

For example, epidemiological studies have shown that prolonged use of aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce the risk of colon ***cancer*** by 40-50% (3). NSAIDs also inhibit chemically induced colon carcinomas in animal model systems (4). Since NSAIDs are known to inhibit cyclooxygenase. . . esters, and growth factors (5, 6). COX-2 expression has recently been shown to be elevated in several different types of human ***cancer*** , suggesting that the presence of COX-2 correlates with ***cancer*** development (7-1 1). Additional studies which directly link COX-2 to carcinogenesis include observations that human colon ***cancer*** cells expressing COX-2 acquire increased invasiveriess (12) and that COX-2 expressed in ***intestinal*** epithelial cells inhibits apoptosis (13). COX-2 expression in colon ***cancer*** cells has also been found to promote angiogenesis of co-cultured endothelial cells by stimulating the production of angiogenic factors (14). Furthermore, direct genetic evidence linking COX-2 to ***colorectal*** ***tumorigenesis*** was provided by a mouse model for human familial adenomatous ***polyposis*** (FA-P), an inherited condition leading to ***colorectal*** ***cancer*** ; in this system, COX-2 gene knockouts and a specific COX-2 inhibitor were found to reduce the number of ***intestinal*** ***polyps*** formed (1 5).

The presence of oncogenic Ras has been associated with the induction of COX-2 expression in H-ras-transformed rat ***intestinal*** and mammary epithelial cellsaswellasinnon-smallcelllungcancercelllines(16-18). Toour knowledge, the association between oncogenic Ras and COX-2 expression has not ben explored in vivo. The high frequency of activating mutations within the K-ras gene in pancreatic ***tumors*** should enable us to investigate the relationship between oncogenic K-ras and COX-2 expression in vivo. In the present study,

we evaluated COX-2 protein levels in primary human pancreatic adenocarcinomas. We further examined whether COX-2 expression correlated with K-ras mutation status in pancreatic ***tumors*** as well as in pancreatic ***cancer*** cell lines. In light of our data demonstrating elevated levels of COX-2 protein in primary pancreatic ***tumors*** and cell lines, we tested the effect of the COX inhibitors sulindac, indomethacin and NS-398 on cell growth and prostaglandin E2 production in human pancreatic ***tumor*** cell lines.

Cyclooxygenase-2 (COX-2) expression is upregulated in several types of human ***cancers*** and has also been directly linked to carcinogenesis. To 1 5 investigate the role of COX-2 in pancreatic ***cancer*** , we evaluated COX-2 protein expression in primary human pancreatic adenocarcinomas (n = 23) and matched normal adjacent tissue (n = I 1) by immunoblot analysis. COX-2 expression was found to be significantly elevated in the pancreatic ***tumor*** specimens compared to normal pancreatic tissue. To examine whether the elevated levels of COX-2 protein observed in pancreatic ***tumors*** correlated with the presence of oncogenic K-ras, we determined the K-ras mutation status in a subset of the ***tumors*** and corresponding non-nal tissues. The presence of oncogenic K-ras did not correlate with the level of COX-2 protein expressed in the pancreatic adenocarcinornas analyzed. These observations were also confirmed in a panel of human pancreatic ***tumor*** cell lines. Furthermore, in the pancreatic ***tumor*** cell line expressing the highest level of COX-2 (BxPC-3), COX-2 expression was demonstrated to be independent of Erkl/2 Map kinase activation. The. . . lack of correlation between COX-2 and oncogenic K-ras expression suggests that Ras activation may not be sufficient to inducing COX-2 expression in pancreatic ***tumor*** cells and that the aberrant activation of signaling pathways other than Ras may be required for up-regulating COX-2 expression. We also. . . report that the COX inhibitors sulindac, indomethacin, and NS-398 inhibited cell growth in both COX positive (BxPC-3) and COX negative (PaCa-2) pancreatic ***tumor*** cell lines. However, suppression of cell growth by indomethacin and NS-398 was sigm icantly greater in the BxPC-3 cell line compared to. . . that COX-2 may play an important role in pancreatic tumongenesis and therefore be a promising chemotherapeutic target for the treatment of pancreatic ***cancer*** .

I 0
Other NSAIDs, including indomethacin and NS-398 also the growth of pancreatic ***tumor*** cell lines, as discussed hereinbelow, and can also be used in the present method, alone, or preferably in combination with sulindac.

. . .
or infusion in dosages of about 500-4000 Mg/M2 /week for up to 7 weeks/cycle for treatment of localized or metastatic pancreatic ***cancer*** (adenocarcinoma of the pancreas). It can also be administered in conjunction with other anti- ***cancer*** agents, such as 5-FU. See, PDR (53rd ed., 1999) at pages 1578

The effect of sulindac or NS-398 alone and in combination with gemcitabine on the growth of pancreatic ***tumor*** cells BxPC-3 and PaCa-2 was investigated. Treatment with the drug combinations inhibited the growth of both cell lines to a greater extent. . . NF-KB DNA binding activity was inhibited by parthenolide treatment. These results suggest that anti-inflammatory drugs may enhance the effectiveness of gemcitabine against pancreatic ***tumors*** .

. . .

of a prophylactic or therapeutic dose of sulindac, an analog thereof or a combination thereof, in the acute or chronic management of ***cancer*** , i.e., pancreatic caner, will vary with the stage of the ***cancer*** , such as the solid ***tumor*** to be treated, the chemotherapeutic agent(s) or other anti- ***cancer*** . therapy used, and the route of administration. The dose, and perhaps the dose frequency, will also vary according to the age, body. . .

. . .

5 chemotherapy regimen. The sulindac, in some cases, may be combined with the same carrier or vehicle used to deliver the anti- ***cancer*** chemotherapeutic agent.

. . .

sterile powders comprising the active ingredient which are adapted for the extemporaneous preparation of sterile injectable or infusible solutions or dispersions, optionally ***encapsulated*** in ***liposomes*** . In all cases, the ultimate dosage form must be sterile, fluid and stable under the conditions of manufacture and storage. The. . . like), vegetable oils, non-toxic glyceryl esters, and suitable mixtures thereof The proper fluidity can be maintained, for example, by the formation of ***liposomes*** , by the maintenance of the required particle size in the case of dispersions or by the use of surfactants. The prevention. . .

. . .

were obtained from the Indiana University Tissue Procurement Laboratory and the Cooperative Human Tissue Network (CHTN) which is funded by the National ***Cancer*** Institute. A total of 23 primary human pancreatic ***cancer*** specimens were analvzed in this study.

. . .

within I hour of surgical removal and subsequently stored at -80'C. Paraffin sections were prepared from a subset of the specimens. All ***tumor*** specimens used in this study were examined by a pathologist and classified as primary pancreatic adenocarcinornas.

5. Statistical Analysis. The presence of statistically significant elevation of COX-2 protein between ***cancer*** specimens and corresponding normal adjacent tissues was determined by the nonparametric signed rank test. A two-way analysis of variance (ANOVA) was used. . .

6. Cell Lines. The human pancreatic ***tumor*** cell lines (AsPC-1, BxPC-3, Capan-1, Capan-2, HPA-F-11, Hs766T, PaCa-2 and PANC-1) were obtained from the American Type Culture Collection (ATCC, Rockville, MD). . .

. . .

Undetectable levels of COX-2 protein were observed in each of the normal specimens. In contrast, COX-2 protein expression in the

pancreatic
5 ***tumor*** tissues ranged from undetectable (sample #2 1) to slight/moderate
(samples #12, 14, 20) to high levels (samples #9, 22). COX-1 protein was observed in both pancreatic ***tumor*** and normal tissues, although the level of
expression was variable and not consistently elevated in the ***tumor*** specimens
(Figure 1). Similar levels of p2l' and actin expression were found in both the
tumor and corresponding normal tissues (Figure 1).

. . .

narrower range (0 3%) of COX-2
expression in the normal tissues. Both the mean and median COX-2 expression
were higher in the ***tumor*** samples, suggesting that COX-2 expression is elevated
in pancreatic adenocarcinomas compared to normal tissue. The difference in
COX-2 expression between the pancreatic ***tumor*** and corresponding normal
tissue was determined to be statistically significant (P = 0.004)
(Figure 2, inset).

. . .

less than 5% respectively, which
corresponds closely with visual detection in the immunoblots. According to
these criteria, 6 out of 11 (55%) ***tumor*** samples in the matched tissue sets were
COX-2 positive. Similarly, 13 out of the 23 (56%) total ***tumor*** specimens
analyzed were COX-2 positive; in contrast, all the normal tissue samples (n
I 1) were COX-2 negative.

h-nmunohistochemical staining of the pancreatic ***tumor*** specimens
demonstrated that COX-2 expression was localized to the carcinoma cells and
was not detectable in the stromal compartment of the ***tumors***
(Figure 3).

Example 2
COX-2 expression and K-ras mutation in pancreatic ***tumors*** and cell lines
To determine if COX-2 expression levels correlated with the K-ras
mutation status of the ***tumors*** , genomic DNA was isolated from a subset of the
tissue specimens and screened for the presence of K-ras mutations at codon. . .

. . .

the
normal tissues analyzed were wild-type at codon 12 (GGT = Gly) and codon 13
(GGC = Gly). Of the 13 pancreatic ***cancer*** specimens analyzed, one specimen
had a mutation at codon 13 whereas IO samples were mutated at codon 12,
corresponding to a K-ras. . . extent of COX-2 protein
expression. For example, some samples expressed high levels of COX-2 protein
and possessed a mutation in K-ras (i.e., ***tumor*** samples #9, 16 and 22); however,
other samples which had mutated K-ras expressed little or no COX-2 protein
(i.e., ***tumor*** samples #3, 17, 18, 19, and 21).

. . .

with known K-ras mutation status (25, 26). Both the frequency and
variability in the quantity of COX-2 expressed in the pancreatic ***tumor*** cell lines
reflected our findings in the primary pancreatic adenocarcinomas. Of the eight
human pancreatic ***tumor*** cell lines analyzed, only three of the seven cell lines
expressing oncogenic K-ras exhibited detectable levels of COX-2 protein

(Capan-1, Capan-2 and. . . (Figure 4B). Taken
together, our results suggest that activation of the Ras pathway is not
sufficient
for mediating COX-2 uprecrulation in pancreatic ***tumor*** cells.
We also compared
the level of COX-2 expression in three hamster pancreatic cell lines,
The
D27/K-ras and B 12/13 transformed cell. . . parental line (Figure 4Q.
These results confirm our conclusion that
Ras activation alone is not sufficient for upregulating COX-2 expression
in
pancreatic ***cancer*** cells and suggest that additional events
which occur following
exposure to chemical carcinogens may be required.

To examine whether COX-2 expression could be induced in the human
pancreatic ***cancer*** cell lines, four cell lines were
serum-starved and subsequently
treated with IO% FCS for various time periods (F1 crure 4D). In. . .
. .
is activated (unpublished observations), again demonstrating
that Erk 1/2 activation is not sufficient for inducing COX-2 expression
in the
COX negative pancreatic ***tumor*** cells. We observed similar
results upon
treating the cell lines with the ***tumor*** promoter, PMA
(unpublished observations).

Example 3
Treatment of pancreatic ***tumor*** cell lines with cyclooxygenase
inhibitors
The COX positive human pancreatic ***tumor*** cell lines, BxPC-3,
and the
COX negative cell line, PaCa-2, were treated with the COX inhibitors
sulindac, indomethacin, or NS Sulindac and. . . was measured after
three days of treatment (Figure 5). All three
inhibitors were found to suppress cell growth in both pancreatic
tumor cell lines
in a dose-dependent manner. However, indomethacin and NS-398 were found
to
inhibit cell growth to a greater extent in the. . .

To evaluate the functional activity of COX-2 in the human pancreatic
tumor cell lines, prostaglandin E2 (PGE,) production was
measured by
enzymeimmunoassay (Figure 6A). PGE2 production was elevated in the BxPC-
3, Capan-1, Capan-2. . .

These data demonstrate that the combination of sulindac and gemcitabine
is more effective than either compound alone in pancreatic ***tumor***
cells.
. . .
as well as inflammatory agents (5, 6,
29). Recent studies have shown that COX-2 expression is upregulated in a
variety of human ***cancers*** , including colon, lung, gastric,
pancreatic and
esophageal (7-1 1). In the present study, we report that
elevated levels of COX-2
protein are expressed in human pancreatic ***tumors*** compared to
barely detectable
levels in the matched non-nal pancreatic tissue, suggesting that
increased
expression of COX-2 protein correlates with pancreatic tunionigenesis.
Our
results confirm a recent report demonstrating upregulation of COX-2 RNA
and
protein in pancreatic ***tumors*** and localization of COX-2 in
malignant epithelial
cells (I 1). An earlier study demonstrated that the expression of group
11
phospholipase A2,. . . phospholipids, was higher in pancreatic ductal
adenocarcinomas
compared to normal pancreatic tissue (30). In addition, the development
of N-

nitrosobis(2-oxopropyl)amine (BOP)-initiated pancreatic ***tumors*** in hamsters was
inhibited bv the administration of two prostaglandin synthesis inhibitors,
phenylbutazone and indomethacin (3 1). Together with our observations
in. . . that increased prostaglandin production due to
the increased expression of COX-2 may be an important event in the multi-step
progression towards pancreatic ***tumor*** formation.
. . .
as well as prostaglandin E2 were detected in Ras-transformed mammary
epithelial cells (C57/MG) cells (I 7). In human non-small cell lung
cancer
(NSCLQ cell lines expressing oncogenic K-Ras, increased PGE2 production was
5 mediated by constitutively high expression of cytosolic, phospholipase A, and
COX-2 compared. . . the expression of detectable levels of
COX-2 protein. A possible explanation for the lack of COX-2 expression in a
subset of the ***tumors*** with oncogenic Ras is that Erkl/2 activity may be down-
regulated in pancreatic carcinomas (26). Moreover, even in the two pancreatic
tumor samples which did show elevated levels of activated Erkl/2 (samples #4
and 21, data not shown), only low levels of COX-2. . . in the present
study, suggesting that Erkl/2 activation alone is not sufficient for inducing
COX-2 expression. These findings suggest that within the ***tumor*** environment,
the presence of oncogenic K-ras does not directly result in increased COX-2
expression in pancreatic ***cancer*** .

Similar conclusions were also reached upon analysis of pancreatic
cancer
cell lines, which were examined since they represent a homogenous population
of cells as opposed to primary ***tumor*** tissue which is heterogenous. Despite
activating K-ras mutations in seven out of the eight lines, only three of the lines
with mutated. . . of COX-2
expression. Activation of other signaling pathways in addition to Ras may
cooperate to determine the extent of COX-2 expression in ***cancer*** cells. Such
pathways may include the p38 mitogen-activated protein kinase which has been
reported to regulate the induction of COX-2 in lipopolysaccharide-
treated. . . the cell type as well as the stimulus. Further experiments will
be required to delineate which signaling pathways are function in pancreatic
tumor cells.
. . .
expressing cell lines. These
data suggest that the COX inhibitors exert their inhibitory effects by both
COX/PGE,-dependent and -independent pathways in pancreatic ***tumor*** cell lines.

The detection of elevated levels of COX-2 in a variety of human
cancers
combined with the chemopreventative effect of NSAIDs in colon
cancer
I 0 demonstrate that COX-2 is an important participant in carcinogenesis. The
reported biological consequences of COX-2 upregulation include inhibition of
apoptosis (13), increased metastatic potential (12) and promotion of anglogenesis
(14). These events may contribute to cell transformation and

tumor progression.

COX-2 expression was noticeably elevated in 55% of the patient pancreatic ***tumor*** samples analyzed, identifying COX-2 as a new target for chemotherapy.

These results demonstratincy the ability of COX inhibitors to inhibit pancreatic ***tumor*** cell growth and PGE, production in vitro indicate that NSAIDs may be effective in the treatment of pancreatic ***cancer*** patients, for whom few treatment options currently exist. COX-2 expression is also useful as a prognostic or diagnostic tool.

1. Landis et al., CA ***Cancer*** J. Clin., 49, 6-29 (1998).

3. Thun, M.J., ***Cancer*** Metastasis Rev., ia, 269-77 (1994).

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8. Ristimaki et al., ***Cancer*** Res., 52, 1276-80 (1997).

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10. Wolff et al., ***Cancer*** Res., 5.-a, 4997-5001 (1998).

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25. Berrozpe et al., Trit. J. ***Cancer*** , 5S, 185-91 (1994).

35. Elder et al., Clin, ***Cancer*** Res-, a, 1679-83 (1997).

36. Piazza et al., ***Cancer*** Res., 52, 2909-15 (1997).

TABLE 1. Analysis of Patient Samples

Tissue Sample'	Tissue Type	% COX-2 b	% ***Cancer***	' K-raE
I	pancreatic adenocarcinorna	7.0	10	WT
2	pancreatic adenocarcinorna	2.0	95	
3	pancreatic adenocarcinoma	0.2	15	GGC to CG,
4	pancreatic adenocarcinorna	3.6. . .	N nornial	0.1 -
12	pancreatic adenocarcinorna	I	15	
14	pancreatic adenocarcinorria	31	ND	

Tissue Sample a	Tissue Type	% COX-2 b	% ***Cancer***	' K-ras
1 5	pancreatic adenocarcinonia	7.8	25	GGT to 15N normal 4.3 - I
1 6	pancreatic adenocarcinoma	66	35	GGT to 16N non-nal. . .

c The percent ***cancer*** was determined by visualization following hematoxylin/eosin staining of slides prepared from paraffin sections.

CLMEN I . A method of reducing the viability of pancreatic ***cancer*** cells comprising contacting the ***cancer*** cells with an effective amount of an NSAID.

2 A method of increasing the susceptibility of mammalian pancreatic ***cancer*** cells to a chemotherapeutic agent comprising contacting the cells with an effective sensitizing amount of an NSAID.

4 The method of claim I or 2 wherein the mammalian ***cancer*** cells are human ***cancer*** cells.

5 The method of claim 3 wherein the sulindac or the analog thereof is administered to a human ***cancer*** patient.

6 The method of claim 5 wherein the ***cancer*** patient is undergoing

treatment with a chemotherapeutic a2ent.

. . .

9 A method of evaluating the ability of sulindac or an analog thereof that is
a COX-2 inhibitor to sensitize pancreatic ***cancer*** cells to a chemotherapeutic
agent comprising:
(a) isolating a first portion of pancreatic ***cancer*** cells from a human
pancreatic ***cancer*** patient;
(b) measuring their viability;
(c) administering sulindac or the analog thereof to said patient;
(d) isolating a second portion of pancreatic ***cancer*** cells from said
patient;
(e) measuring the viability of the second portion of pancreatic ***cancer***
cells; and
(f) comparing the viability measured in step (e) with the viability measured in step (b); wherein reduced viability in step (e) indicates. . .

. . .

T N T
COX-2 mm 40- cwIlw
C OX- 1
p2i ras
Actin
]1]] VW lwo ow
C/ (]-)
/8
loo -
90 - lo(
9CF
80-
9
7CF
70-
60-
40
3Y
to 50-
a
cw
C*4 26
40- 1 Cy
0
TUMOR NORMAL
30 -
20-
lo-
8
0- 00
TUMOR NORMAL
(n--23)
y1wMian = 5.2% median = 02%
nwan = 15.2 +/- 24.9% mcan 0.83 +/- 1.3%
v2mge = 0 - 93% map 0. . . Sulindac IndometIL NS-398
% inhibition: 0 07 90 F957 98 759 86
/8
Effect of Sulindac + Gemcitabine on the growth of the pancreatic ***tumor*** cell line, BxPC-3 (day 3)
125 -
100 I Gem alone
75 -
1,100+ e
50 - T
em
sul, 500 + Gem
0 5 10 15 20. . . and Technology Institute, Inc.
Marshall, Mark Steven
Sweeney, Christopher J.
Yip-Schneider, Michele T.
Crowell, Pamela L.
10<120> Use of NSAIDs for the treatment of pancreatic ***cancer***

<130> 740.018WO1
<150> US 60/165,543
15<151> 1999 15
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<210> 2
30<211>. . . search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ,, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS, ***CANCERLIT***
C. DOCUMENTS CONSIDERED TO BE RELEVANT
Category Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.
PqX SWEENEY J. ET AL.: INHIBITION OF CELL 1-11
GROWTH IN PANCREATIC ***TUMOR*** CELLS BY
ANTI-INFLAMMATORA DRUGS11
PROCEEDINGS OF THE AMERICAN ASSOCIATION
FOR ***CANCER*** RESEARCH,
vol. 41, March 2000 (2000-03),, page 527
XPOO2164391
USA
ABSTRACT #3358
abstract
Further documents are listed in the continuation of box C. Patent family members. . . passages Relevant to claim NO.
PqX MARSHALL M.S. ET AL.: SUPPRESSION OF 1-11
PANCREATIC DUCTAL ADENOCARCINOMA GROWTH BY
SULINDACH
PROCEEDINGS OF THE AMERICAN ASSOCIATION
FOR ***CANCER*** RESEARCH,
vol. 41, March 2000 (2000-03), page 526
XPOO2164392
USA
ABSTRACT #3349
abstract
P9X T.YIP-SCHNEIDER M. ET AL.: COX-2 1-11
EXPRESSION IN HAMAN PANCREATIC
ADENOCARCINOMAS11
CARCINOGENESIS,
vol. 21, no. 2,. . . XPOO0984815
the whole document
X MOLINA M, ET AL.: INCREASED COX-2 1-11
EXPRESSION IN HUMAN PANCREATIC CARCINOMAS
AND CELL LINES: GROWTH INHIBITION NY
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS11
CANCER RESEARCH,
vol. 59, no. 17, September 1999 (1999-09),
pages 4356-4362, XPOO0984712
the whole document
X WO 99 49859 A (THE ARIZONA BOARD OF 1-698
REGENTS). . .

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---Logging off of STN---

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=> s microspher?
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L4       1026 L2 OR L3

=> s polyanhydride
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L5      6164 POLYANHYDRIDE
             (POLYANHYDRIDE OR POLYANHYDRIDES)

=> s sulindac
L6       2826 SULINDAC

=> s l6 and l4
L7         16 L6 AND L4

=> s l7 and l5
L8          3 L7 AND L5

=> d ibib 1-3

L8    ANSWER 1 OF 3    PCTFULL   COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:       2005081825 PCTFULL  ED 20050914  EW 200536
TITLE (ENGLISH):        ABUSE RESISTANT OPIOID TRANSDERMAL DELIVERY DE'
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TITLE (FRENCH):         DISPOSITIF DE DISTRIBUTION TRANSDERMIQUE D'OPIOI[
                        EMPECHANT UNE UTILISATION ABUSIVE ET CONTENANT DES
                          ***MICROSPHERES***   D'ANTAGONISTES D'OPIOIDES
INVENTOR(S):            REIDENBERG, Bruce, 1 Stonycrest Road, Rye, NY 01580, US
                        [US, US];
                        SHEVCHUK, Ihor, 11 Shelburne Road, Yonkers, NY 10710,
                        US [US, US];
                        TAVARES, Lino, 86 South Glen Road, Kinnelon, NJ 07405,
                        US [US, US];
                        LONG, Kevin, 3 Hidden Hill Road, Oak Ridge, NJ 07438,
                        US [US, US];
                        MASKIEWICZ, Richard, 88 Saunders Lane, Richfield, CT
                        06877, US [US, US];
                        SHAMEEM, Mohammed, 4 Surim Court, Nanuet, NY 10954, US
                        [US, US]
PATENT ASSIGNEE(S):     EURO-CELTIQUE S.A., 122, Boulevard de la Petrusse,
                        L-2330 Luxembourg, LU [LU, LU], for all designates
                        States except US;
                        REIDENBERG, Bruce, 1 Stonycrest Road, Rye, NY 01580, US
                        [US, US], for US only;
                        SHEVCHUK, Ihor, 11 Shelburne Road, Yonkers, NY 10710,
                        US [US, US], for US only;
                        TAVARES, Lino, 86 South Glen Road, Kinnelon, NJ 07405,
                        US [US, US], for US only;
                        LONG, Kevin, 3 Hidden Hill Road, Oak Ridge, NJ 07438,
                        US [US, US], for US only;
```

MASKIEWICZ, Richard, 88 Saunders Lane, Richfield, CT 06877, US [US, US], for US only;
SHAMEEM, Mohammed, 4 Surim Court, Nanuet, NY 10954, US [US, US], for US only
AGENT: DAVIDSON, Clifford, M.$, Davidson, Davidson & Kappel, LLC, 485 Seventh Avenue, 14th Floor, New York, NY 10018$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005081825	A2	20050909

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PRIORITY INFO.: US 2004-60/547,196 20040223

L8 ANSWER 2 OF 3 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2004052339 PCTFULL ED 20040630 EW 200426
TITLE (ENGLISH): PH TRIGGERED TARGETED CONTROLLED RELEASE SYST
TITLE (FRENCH): SYSTEMES DE LIBERATION CONTROLEE CIBLEE A DECLE FONCTION DU PH
INVENTOR(S): SHEFER, Adi, 14 Jason Drive, East Brunswick, NJ 08816, US;
SHEFER, Samuel, David, 14 Jason Drive, East Brunswick, NJ 08816, US
PATENT ASSIGNEE(S): SALVONA LLC, 65 Stults Road, Dayton, NJ 08810, US [US US]
AGENT: DUNN, McKay, Diane$, Mathews, Collins, Shepherd & McKay, P.A., 100 Thanet Circle, Suite 306, Priceton, NJ 08540$, US
LANGUAGE OF FILING: English
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PRIORITY INFO.: US 2002-10/315,801 20021209

L8 ANSWER 3 OF 3 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1996040090 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD FOR REDUCING OR PREVENTING POST-SURGIC ADHESION FORMATION USING 5-LIPOXYGENASE INHIBITORS
TITLE (FRENCH): PROCEDE POUR LA REDUCTION OU LA PREVENTION DE FORMATION D'ADHERENCES POST-CHIRURGICALES A L'AIDE D'INHIBITEURS DE 5-LIPOXYDASE
INVENTOR(S): RODGERS, Kathleen, Elizabeth;
diZEREGA, Gere, Stodder
PATENT ASSIGNEE(S): UNIVERSITY OF SOUTHERN CALIFORNIA

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LANGUAGE OF PUBL.:      English
DOCUMENT TYPE:          Patent
PATENT INFORMATION:
                NUMBER          KIND    DATE
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                WO 9640090          A1 19961219
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                PT SE
APPLICATION INFO.:      WO 1996-US8216      A  19960531
PRIORITY INFO.:         US 1995-8/473,183       19950607


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L4         1026 S L2 OR L3
L5         6164 S POLYANHYDRIDE
L6         2826 S SULINDAC
L7           16 S L6 AND L4
L8            3 S L7 AND L5

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       189307 POLYMER
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          178 POLYMERICS
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L17         16 L16 AND L7

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L18   ANSWER 1 OF 11   PCTFULL  COPYRIGHT 2005 Univentio on STN
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TITLE (FRENCH):        ***MICROSPHERES***  PERMETTANT UNE EMBOLISATIC
                       ACTIVE
INVENTOR(S):           VOGEL, Jean-Marie;
                       BOSCHETTI, Egisto
PATENT ASSIGNEE(S):    BIOSPHERE MEDICAL INC.;
                       VOGEL, Jean-Marie;
                       BOSCHETTI, Egisto
DOCUMENT TYPE:         Patent
PATENT INFORMATION:
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                       MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ
                       TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ
                       SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH
                       CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ
                       CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:     WO 2001-US9619      A  20010323
PRIORITY INFO.:        US 2000-60/191,899     20000324

L18   ANSWER 2 OF 11   PCTFULL  COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:      2001072280 PCTFULL  ED 20020822
TITLE (ENGLISH):       ***MICROSPHERES***  FOR GENE THERAPY
TITLE (FRENCH):        COMPOSITIONS ET METHODES POUR THERAPIE GENIQU
INVENTOR(S):           VOGEL, Jean-Marie;
                       BOSCHETTI, Egisto
PATENT ASSIGNEE(S):    BIOSPHERE MEDICAL INC.;
                       VOGEL, Jean-Marie;
                       BOSCHETTI, Egisto
DOCUMENT TYPE:         Patent
PATENT INFORMATION:
                       NUMBER          KIND    DATE
                       --------------------------------
                       WO 2001072280       A2 20011004
DESIGNATED STATES
     W:                 AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
                       CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL
                       IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG
                       MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ
                       TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ
                       SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH
                       CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ
                       CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:     WO 2001-US9618      A  20010323
PRIORITY INFO.:        US 2000-60/191,902     20000324

L18   ANSWER 3 OF 11   PCTFULL  COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:      2001070291 PCTFULL  ED 20020822
TITLE (ENGLISH):       INJECTABLE  ***MICROSPHERES***  FOR DERMAL
                       AUGMENTATION AND TISSUE BULKING
TITLE (FRENCH):        ***MICROSPHERES***  INJECTABLES DESTINEES A
                       L'AUGMENTATION DERMIQUE ET AU GONFLEMENT TISSULAIRE
INVENTOR(S):           VOGEL, Jean-Marie;
                       THOMAS, Richard;
                       BOSCHETTI, Egisto
PATENT ASSIGNEE(S):    BIOSPHERE MEDICAL, INC.
DOCUMENT TYPE:         Patent
PATENT INFORMATION:
                       NUMBER          KIND    DATE
                       --------------------------------
                       WO 2001070291       A2 20010927
DESIGNATED STATES
```

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    W:          AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
                CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL
                IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG
                MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ
                TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD
                SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
                DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
                CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:    WO 2001-US8529      A  20010315
PRIORITY INFO.:       US 2000-09/528,991     20000320

L18   ANSWER 4 OF 11   PCTFULL  COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:     2001070289 PCTFULL  ED 20020822
TITLE (ENGLISH):      INJECTABLE AND SWELLABLE  ***MICROSPHERES***  FC
                TISSUE BULKING
TITLE (FRENCH):       ***MICROSPHERES***  INJECTABLES, SUSCEPTIBLES DI
                FOISONNEMENT, VISANT A FAIRE GONFLER UN TISSU
INVENTOR(S):          VOGEL, Jean-Marie;
                BOSCHETTI, Egisto
PATENT ASSIGNEE(S):   BIOSPHERE MEDICAL, INC.
DOCUMENT TYPE:        Patent
PATENT INFORMATION:
                NUMBER          KIND    DATE
                ----------------------------
                WO 2001070289       A2 20010927
DESIGNATED STATES
    W:          AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
                CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL
                IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG
                MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ
                TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD
                SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
                DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
                CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:    WO 2001-US8405      A  20010315
PRIORITY INFO.:       US 2000-09/528,989     20000320

L18   ANSWER 5 OF 11   PCTFULL  COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:     2000024378 PCTFULL  ED 20020515
TITLE (ENGLISH):      COMPOSITIONS OF  ***MICROSPHERES***  FOR WOUND
                HEALING
TITLE (FRENCH):       COMPOSITIONS A BASE DE  ***MICROSPHERES***  DEST
                AU TRAITEMENT DES BLESSURES
INVENTOR(S):          RITTER, Vladimir;
                RITTER, Marina
PATENT ASSIGNEE(S):   POLYHEAL LTD;
                RITTER, Vladimir;
                RITTER, Marina
LANGUAGE OF PUBL.:    English
DOCUMENT TYPE:        Patent
PATENT INFORMATION:
                NUMBER          KIND    DATE
                ----------------------------
                WO 2000024378       A1 20000504
DESIGNATED STATES
    W:          AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE
                ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK
                LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD
                SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM
                KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE
                CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ
                CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:    WO 1998-IB1838      A  19981023


=> d ibib 6-10

L18   ANSWER 6 OF 11   PCTFULL  COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:     1998051284 PCTFULL  ED 20020514
TITLE (ENGLISH):      NOVEL ACOUSTICALLY ACTIVE DRUG DELIVERY SYSTEM
TITLE (FRENCH):       NOUVEAUX SYSTEMES D'ADMINISTRATION DE MEDICAM
                ACTIVES PAR UN PROCEDE ACOUSTIQUE
INVENTOR(S):          UNGER, Evan, C.
PATENT ASSIGNEE(S):   IMARX PHARMACEUTICAL CORP.
```

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9851284	A1	19981119

DESIGNATED STATES
W: AU BR CA CN JP KR NZ AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US9569 A 19980512
PRIORITY INFO.: US 1997-60/046,379 19970513
US 1998-9/075,343 19980511

L18 ANSWER 7 OF 11 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1996040090 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD FOR REDUCING OR PREVENTING POST-SURGIC ADHESION FORMATION USING 5-LIPOXYGENASE INHIBITORS
TITLE (FRENCH): PROCEDE POUR LA REDUCTION OU LA PREVENTION DE FORMATION D'ADHERENCES POST-CHIRURGICALES A L'AIDE D'INHIBITEURS DE 5-LIPOXYDASE
INVENTOR(S): RODGERS, Kathleen, Elizabeth;
diZEREGA, Gere, Stodder
PATENT ASSIGNEE(S): UNIVERSITY OF SOUTHERN CALIFORNIA
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9640090	A1	19961219

DESIGNATED STATES
W: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1996-US8216 A 19960531
PRIORITY INFO.: US 1995-8/473,183 19950607

L18 ANSWER 8 OF 11 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1995015118 PCTFULL ED 20020514
TITLE (ENGLISH): GAS ***MICROSPHERES*** FOR TOPICAL AND SUBCUT/ APPLICATION
TITLE (FRENCH): ***MICROSPHERES*** GAZEUSES POUR APPLICATION TOPIQUE ET SOUS-CUTANEE
INVENTOR(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David
PATENT ASSIGNEE(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9515118	A1	19950608

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US13817 A 19941130
PRIORITY INFO.: US 1993-8/159,674 19931130
US 1993-8/159,687 19931130
US 1993-8/160,232 19931130
US 1994-8/307,305 19940916
US 1994-8/346,426 19941129

L18 ANSWER 9 OF 11 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1994028874 PCTFULL ED 20020513
TITLE (ENGLISH): NOVEL THERAPEUTIC DELIVERY SYSTEMS
TITLE (FRENCH): NOUVEAU SYSTEME D'ADMINISTRATION DE PRODUITS THERAPEUTIQUES
INVENTOR(S): UNGER, Evan, C.;
FRITZ, Thomas, A.;
MATSUNAGA, Terry;
RAMASWAMI, VaradaRajan;
YELLOWHAIR, David;
WU, Guanli

PATENT ASSIGNEE(S): UNGER, Evan, C.;
FRITZ, Thomas, A.;
MATSUNAGA, Terry;
RAMASWAMI, VaradaRajan;
YELLOWHAIR, David;
WU, Guanli
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9428874	A1	19941222

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL
PT SE
APPLICATION INFO.: WO 1994-US5633 A 19940519
PRIORITY INFO.: US 1993-8/076,250 19930611
US 1993-8/159,674 19931130
US 1993-8/159,687 19931130
US 1993-8/160,232 19931130

L18 ANSWER 10 OF 11 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1994028873 PCTFULL ED 20020513
TITLE (ENGLISH): NOVEL THERAPEUTIC DRUG DELIVERY SYSTEMS
TITLE (FRENCH): NOUVEAUX SYSTEMES D'ADMINISTRATION DE MEDICAMI
INVENTOR(S): UNGER, Evan, C.;
FRITZ, Thomas, A.;
MATSUNAGA, Terry;
RAMASWAMI, VaradaRajan;
YELLOWHAIR, David;
WU, Guanli
PATENT ASSIGNEE(S): UNGER, Evan, C.;
FRITZ, Thomas, A.;
MATSUNAGA, Terry;
RAMASWAMI, VaradaRajan;
YELLOWHAIR, David;
WU, Guanli
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9428873	A1	19941222

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL
PT SE
APPLICATION INFO.: WO 1994-US5620 A 19940512
PRIORITY INFO.: US 1993-8/076,250 19930611

=> d kwic 10

L18 ANSWER 10 OF 11 PCTFULL COPYRIGHT 2005 Univentio on STN
ABEN Therapeutic drug delivery sytems comprising gas-filled
microspheres comprising a therapeutic
are described. Methods for employing such ***microspheres*** in
therapeutic drug delivery applications are
also provided. Drug delivery systems comprising gas-filled liposomes
having encapsulated therein a
drug are. . .
ABFR Systemes d'administration de medicaments au moyen de
microspheres remplies d'un gaz a effet
therapeutique, et methodes d'utilisation associees. Sont preconises des
systemes d'administration a
base de liposomes remplis. . .

DETD . . . deliver genetic material to
5 living cells. These mechanisms include techniques such as
calcium phosphate precipitation and electroporation, and
carriers such as cationic ***polymers*** and aqueous-filled
liposomes. These methods have all been relatively
ineffective in vivo and only of limited use for cell culture
transfection. None of. . .
. . .

such as ganglioside GM1
and GM2; glucolipids; sulfatides; glycosphingolipids;
- 14 -
phosphatidic acid; palmitic acid; stearic acid; arachidonic
acid; oleic acid; lipids bearing ***polymers*** such as
polyethyleneglycol, chitin, hyaluronic acid or
polyvinylpyrrolidone; lipids bearing sulfonated mono-, di-,
5 oligo- or polysaccharides; cholesterol, cholesterol sulfate
and cholesterol hemisuccinate; tocopherol. . .
. . .
microsphere. Preferably, this
non-cationic lipid is dipalmitoylphosphatidylcholine,
- 15 -
dipalmitoylphosphatidylethanolamine or dioleoylphosphatidyl-
ethanolamine. In lieu of cationic lipids as described above,
lipids bearing cationic ***polymers*** such as polylysine or
polyarginine may also be used to construct the microspheres
5 and afford binding of a negatively charged therapeutic,. . .
. . .
to
carbohydrates and their phosphorylated and sulfonated
derivatives; polyethers, preferably with molecular weight
ranges between 400 and 8000; di- and trihydroxy alkanes and
their ***polymers*** , preferably with molecular weight ranges
between 800 and 8000. Emulsifying and/or solubilizing agents
may also be used in conjunction with lipids or. . .
. . .
methicillin, nafcillin, oxacillin, penicillin G, penicillin
V, ticarcillin rifampin and tetracycline; antiinflammatories
such as diflunisal, ibuprofen, indomethacin, meclofenamate,
mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone,
piroxicam, ***sulindac*** , tolmetin, aspirin and salicylates;
20 antiprotozoans such as chloroquine, hydroxychloroquine,
metronidazole, quinine and meglumine antimonate;
antirheumatics such as penicillamine; narcotics such as
paregoric; opiates. . .
. . .
DNA and analogs thereof, such as
20 phosphorothioate and phosphorodithioate
oligodeoxynucleotides. Additionally, the genetic material
may be combined, for example, with proteins or other
polymers .
. . .
form the microspheres include, for example, proteins
such as albumin, synthetic peptides such as polyglutamic
acid, and linear and branched oligomers and ***polymers*** of
- 25 -
galactose, glucose and other hexosaccharides and ***polymers***
derived from phosphorylated and sulfonated pentose and hexose
sugars and sugar alcohols. Carbohydrate ***polymers*** such as
alginic acid, dextran, starch and HETA starch may also be
5used. Other natural ***polymers*** , such as hyaluronic acid, may
be utilized. Synthetic ***polymers*** such as polyethyleneglycol,
polyvinylpyrrolidone, polylactide, polyethyleneimines (linear
and branched), polyionenes or polyiminocarboxylates may also
be employed.

=> d his

(FILE 'HOME' ENTERED AT 08:21:20 ON 15 DEC 2005)

FILE 'PCTFULL' ENTERED AT 08:21:30 ON 15 DEC 2005
L1 15203 S MICROSPHER?
L2 343 S L1/TI
L3 990 S L1/AB
L4 1026 S L2 OR L3
L5 6164 S POLYANHYDRIDE
L6 2826 S SULINDAC
L7 16 S L6 AND L4
L8 3 S L7 AND L5
L9 16 S L7 AND POLYMER
L10 12 S L7 NOT PY>2002
L11 90719 S CANCER? OR TUMOR? OR CANCER?

```
L12        12 S L11 AND L10
L13     89307 S POLYMERIC
L14     89310 S L13 OR L9
L15    189307 S POLYMER
L16    208045 S L15 OR L13
L17        16 S L16 AND L7
L18        11 S L17 NOT PY>2001

=>

---Logging off of STN---


=>
Executing the logoff script...

=> LOG Y

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * * * *  Welcome to STN International  * * * * * * * * * * * *

 NEWS  1        Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2        "Ask CAS" for self-help around the clock
 NEWS  3  JAN 17  Pre-1988 INPI data added to MARPAT
 NEWS  4  FEB 21  STN AnaVist, Version 1.1, lets you share your STN AnaVist
          visualization results
 NEWS  5  FEB 22  The IPC thesaurus added to additional patent databases on STN
 NEWS  6  FEB 22  Updates in EPFULL; IPC 8 enhancements added
 NEWS  7  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS  8  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS  9  MAR 22  EMBASE is now updated on a daily basis
 NEWS 10  APR 03  New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 11  APR 03  Bibliographic data updates resume; new IPC 8 fields and IPC
          thesaurus added in PCTFULL
 NEWS 12  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS 13  APR 12  LINSPEC, learning database for INSPEC, reloaded and enhancec
 NEWS 14  APR 12  Improved structure highlighting in FQHIT and QHIT display
          in MARPAT
 NEWS 15  APR 12  Derwent World Patents Index to be reloaded and enhanced during
          second quarter; strategies may be affected
 NEWS 16  MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS 17  MAY 11  KOREAPAT updates resume
 NEWS 18  MAY 19  Derwent World Patents Index to be reloaded and enhanced

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
          CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
          AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
          V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
          http://download.cas.org/express/v8.0-Discover/

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available after June 2006

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specific topic.

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like to better understand what you find useful. Please take
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If you provide us with your name, login ID, and e-mail address, you
will be entered in a drawing to win a free iPod(R). Your responses
will be kept confidential and will help us make future improvements
to STN.

***Take survey: http://www.zoomerang.com/survey.zgi?p=WEB2259HNKWTUW ***

Thank you in advance for your participation.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:54:10 ON 23 MAY 2006

=> file reg
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 14:54:22 ON 23 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 MAY 2006 HIGHEST RN 885262-53-3
DICTIONARY FILE UPDATES: 22 MAY 2006 HIGHEST RN 885262-53-3

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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```
*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005. A new display format, IDERL, is now         *
* available and contains the CA role and document type information.     *
*                                                                       *
*************************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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=> E "SULINDAC"/CN 25
E1        1    SULIKOL K/CN
E2        1    SULIN/CN
E3        1 --> SULINDAC/CN
E4        1    SULINDAC B .OMEGA.-N-METHYL-L-ARGININE SALT/CN
```

```
E5        1    SULINDAC B .OMEGA.-N-NITRO-L-ARGININE METHYL ESTER SALT/
E6        1    SULINDAC B .OMEGA.-N-NITRO-L-ARGININE SALT/CN
E7        1    SULINDAC ETHYL ESTER/CN
E8        1    SULINDAC SODIUM/CN
E9        1    SULINDAC SULFIDE/CN
E10       1    SULINDAC SULFONE/CN
E11       1    SULINDAC SULFOXIDE/CN
E12       1    SULINDAC-QUINOLINE/CN
E13       1    SULINEX/CN
E14       1    SULINOL/CN
E15       1    SULIODOVIZOL/CN
E16       1    SULISATIN/CN
E17       1    SULISATIN DISODIUM SALT/CN
E18       1    SULISATIN SODIUM/CN
E19       1    SULISATINE SODIUM/CN
E20       1    SULISOBENZONE/CN
E21       1    SULJEX/CN
E22       1    SULKA/CN
E23       1    SULKA K BOLUSES/CN
E24       1    SULKA N/CN
E25       1    SULKOR/CN

=> S E3
L1        1 SULINDAC/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN  38194-50-2  REGISTRY
CN  1H-Indene-3-acetic acid, 5-fluoro-2-methyl-1-[[4-
    (methylsulfinyl)phenyl]methylene]-, (1Z)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN  1H-Indene-3-acetic acid, 5-fluoro-2-methyl-1-[[4-
    (methylsulfinyl)phenyl]methylene]-, (Z)-
OTHER NAMES:
CN  Aflodac
CN  Algocetil
CN  Arthrocine
CN  Artribid
CN  cis-5-Fluoro-2-methyl-1-[(p-methylsulfinyl)benzylidenyl]indene-3-acetic
    acid
CN  cis-Sulindac
CN  Citireuma
CN  Clinoril
CN  Clisundac
CN  Imbaral
CN  MK 231
CN  Mobilin
CN  Reumofil
CN  Reumyl
CN  Sudac
CN  ***Sulindac***
CN  Sulindac sulfoxide
CN  Sulinol
CN  Sulreuma
FS  STEREOSEARCH
DR  49627-22-7
MF  C20 H17 F O3 S
CI  COM
LC  STN Files:  ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECH
    CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDF
    DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSPATENTS, IPA
    MEDLINE, MRCK*, MSDS-OHS, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCI
    SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
      (*File contains numerically searchable property data)
    Other Sources:  EINECS**, WHO
      (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Conference; Dissertation; Journal; Patent
RL.P  Roles from patents:  ANST (Analytical study); BIOL (Biological study);
    PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
    reagent); USES (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
```

study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Double bond geometry as shown.

/ Structure 1 in file .gra /

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1474 REFERENCES IN FILE CA (1907 TO DATE)
77 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1477 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 7.10 7.31

FILE 'CAPLUS' ENTERED AT 14:55:07 ON 23 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 23 May 2006 VOL 144 ISS 22
FILE LAST UPDATED: 22 May 2006 (20060522/ED)

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=> s l1
L2 1477 L1

=> IL-12 or IL12 or (IL 12)
IL-12 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s IL-12 or IL12 or (IL 12)
114245 IL
1077 ILS
115018 IL
(IL OR ILS)
1386581 12
9806 IL-12
(IL(W)12)
844 IL12
114245 IL
1077 ILS
115018 IL

```
          (IL OR ILS)
     1386581 12
       9806 IL 12
          (IL(W)12)
L3      10023 IL-12 OR IL12 OR (IL 12)

=> s l3 and l1
        1477 L1
L4         4 L3 AND L1

=> s l2 and l3
L5         4 L2 AND L3

=> s l2 (L) l3
L6         1 L2 (L) L3

=> d ibib

L6  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:       2005:823135  CAPLUS
DOCUMENT NUMBER:        143:210437
TITLE:                  Autologous human dendritic cells fused with autologous
                        cancer cells and human IL-12 for combined
                        immunotherapy of cancer
INVENTOR(S):            Ohno, Tsuneya
PATENT ASSIGNEE(S):     USA
SOURCE:                 U.S. Pat. Appl. Publ., 51 pp.
                        CODEN: USXXCO
DOCUMENT TYPE:          Patent
LANGUAGE:               English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

    PATENT NO.         KIND   DATE       APPLICATION NO.       DATE
    --------------     ----   --------   -------------------   --------
    US 2005180951       A1    20050818   US 2004-778717        20040212
    WO 2005079271       A2    20050901   WO 2005-US4237        20050211
       W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
           CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
           GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
           LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
           NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
           TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
       RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
           AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
           EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
           RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
           MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2004-778717     A  20040212


=> d l5 ibib 1-4

L5  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:       2005:823135  CAPLUS
DOCUMENT NUMBER:        143:210437
TITLE:                  Autologous human dendritic cells fused with autologous
                        cancer cells and human  ***IL***  -  ***12***  for
                        combined immunotherapy of cancer
INVENTOR(S):            Ohno, Tsuneya
PATENT ASSIGNEE(S):     USA
SOURCE:                 U.S. Pat. Appl. Publ., 51 pp.
                        CODEN: USXXCO
DOCUMENT TYPE:          Patent
LANGUAGE:               English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

    PATENT NO.         KIND   DATE       APPLICATION NO.       DATE
    --------------     ----   --------   -------------------   --------
    US 2005180951       A1    20050818   US 2004-778717        20040212
    WO 2005079271       A2    20050901   WO 2005-US4237        20050211
       W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
           CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2004-778717 A 20040212

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:591975 CAPLUS
DOCUMENT NUMBER: 143:53482
TITLE: Method for inhibiting the growth of gastrointestinal tract tumors
INVENTOR(S): Egilmez, Nejat K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147689	A1	20050707	US 2003-748003	20031230
CA 2491338	AA	20050630	CA 2004-2491338	20041223

PRIORITY APPLN. INFO.: US 2003-748003 A 20031230

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:570530 CAPLUS
DOCUMENT NUMBER: 143:91017
TITLE: Use of anti-inflammatory agent, anti-rheumatic agent, antihistamine and immunosuppressor in conjunction with liposome-mediated gene therapy to reduce inflammation
INVENTOR(S): Ramesh, Rajagopal; Gopalan, Began; Roth, Jack A.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: U.S. Pat. Appl. Publ., 61 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005143336	A1	20050630	US 2004-341	20041130

PRIORITY APPLN. INFO.: US 2003-533180P P 20031230

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:119752 CAPLUS
DOCUMENT NUMBER: 140:162347
TITLE: Compositions comprising tumor-dendritic Fusion cells, recombinant human interleukin 12, antipyretic and immunosuppressant for cancer immunotherapy
INVENTOR(S): Ohno, Tsuneya
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. Ser. No. 12,134.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004028663	A1	20040212	US 2002-328998	20021224
US 2002168351	A1	20021114	US 2001-12134	20011022

PRIORITY APPLN. INFO.: US 2000-242154P P 20001020
US 2001-12134 A2 20011022

```
=> s COX2 or (COX-2) or (COX 2)
        3949 COX2
       19709 COX
          2 COXES
       19711 COX
             (COX OR COXES)
     8741746 2
       10212 COX-2
             (COX(W)2)
       19709 COX
          2 COXES
       19711 COX
             (COX OR COXES)
     8741746 2
       10212 COX 2
             (COX(W)2)
L7      11606 COX2 OR (COX-2) OR (COX 2)

=> d his

    (FILE 'HOME' ENTERED AT 14:54:10 ON 23 MAY 2006)

    FILE 'REGISTRY' ENTERED AT 14:54:22 ON 23 MAY 2006
            E "SULINDAC"/CN 25
L1           1 S E3

    FILE 'CAPLUS' ENTERED AT 14:55:07 ON 23 MAY 2006
L2        1477 S L1
L3       10023 S IL-12 OR IL12 OR (IL 12)
L4           4 S L3 AND L1
L5           4 S L2 AND L3
L6           1 S L2 (L) L3
L7       11606 S COX2 OR (COX-2) OR (COX 2)

=> s l7 and l3
L8          45 L7 AND L3

=> s l7 (L) l3
L9          39 L7 (L) L3

=> s synerg
=> s synerg?
L10     104630 SYNERG?

=> s l10 and l8
L11          0 L10 AND L8

=> s l10 and l9
L12          0 L10 AND L9

=> s l3 and l10
L13        645 L3 AND L10

=> s l13 and NSAID?
        7454 NSAID?
L14          0 L13 AND NSAID?

=> file pctfull
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                    ENTRY   SESSION
FULL ESTIMATED COST                             32.78      40.09

FILE 'PCTFULL' ENTERED AT 15:00:05 ON 23 MAY 2006
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FILE LAST UPDATED:        23 MAY 2006      <20060523/UP>
MOST RECENT UPDATE WEEK:       200620       <200620/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
   SEE
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   http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
   (last updated April 10, 2006) <<<

=> s sulindac or clinoril or aflodac or mobilin
        3129 SULINDAC
         112 CLINORIL
           1 CLINORILS
         113 CLINORIL
             (CLINORIL OR CLINORILS)
           0 AFLODAC
           1 MOBILIN
L15      3143 SULINDAC OR CLINORIL OR AFLODAC OR MOBILIN

=> s COX2 or (COX-2) or (COX 2)
         500 COX2
       10544 COX
     1011013 2
        4012 COX-2
             (COX(W)2)
       10544 COX
     1011013 2
        4012 COX 2
             (COX(W)2)
L16      4331 COX2 OR (COX-2) OR (COX 2)

=> s synerg
L17        55 SYNERG

=> s synerg?
L18     35843 SYNERG?

=> s l16/ab
          12 COX2/AB
         374 COX/AB
      207883 2/AB
         296 COX-2/AB
             ((COX(W)2)/AB)
         374 COX/AB
      207883 2/AB
         296 COX 2/AB
             ((COX(W)2)/AB)
L19       304 (COX2/AB OR (COX-2/AB) OR (COX 2/AB))

=> s l19 and l18
L20        65 L19 AND L18

=> s IL-12 or IL12 or (IL 12)
      301684 IL
       55063 ILS
      320462 IL
             (IL OR ILS)
      911008 12
        6676 IL-12
             (IL(W)12)
         582 IL12
      301684 IL
       55063 ILS
      320462 IL
             (IL OR ILS)
      911008 12
        6676 IL 12
             (IL(W)12)
L21      6900 IL-12 OR IL12 OR (IL 12)

=> s l21 and l20
L22         7 L21 AND L20

=> s l21/clm
       72231 IL/CLM
      722730 12/CLM
         992 IL-12/CLM
             ((IL(W)12)/CLM)
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        59 IL12/CLM
     72231 IL/CLM
    722730 12/CLM
       992 IL 12/CLM
           ((IL(W)12)/CLM)
L23     1033 (IL-12/CLM OR IL12/CLM OR (IL 12/CLM))

=> s l23 and l18
L24      284 L23 AND L18

=> d his

   (FILE 'HOME' ENTERED AT 14:54:10 ON 23 MAY 2006)

   FILE 'REGISTRY' ENTERED AT 14:54:22 ON 23 MAY 2006
          E "SULINDAC"/CN 25
L1          1 S E3

   FILE 'CAPLUS' ENTERED AT 14:55:07 ON 23 MAY 2006
L2       1477 S L1
L3      10023 S IL-12 OR IL12 OR (IL 12)
L4          4 S L3 AND L1
L5          4 S L2 AND L3
L6          1 S L2 (L) L3
L7      11606 S COX2 OR (COX-2) OR (COX 2)
L8         45 S L7 AND L3
L9         39 S L7 (L) L3
L10    104630 S SYNERG?
L11         0 S L10 AND L8
L12         0 S L10 AND L9
L13       645 S L3 AND L10
L14         0 S L13 AND NSAID?

   FILE 'PCTFULL' ENTERED AT 15:00:05 ON 23 MAY 2006
L15      3143 S SULINDAC OR CLINORIL OR AFLODAC OR MOBILIN
L16      4331 S COX2 OR (COX-2) OR (COX 2)
L17        55 S SYNERG
L18     35843 S SYNERG?
L19       304 S L16/AB
L20        65 S L19 AND L18
L21      6900 S IL-12 OR IL12 OR (IL 12)
L22         7 S L21 AND L20
L23      1033 S L21/CLM
L24       284 S L23 AND L18

=> s l24 and l15
L25        22 L24 AND L15

=> s l15/clm
       490 SULINDAC/CLM
         9 CLINORIL/CLM
         0 AFLODAC/CLM
         0 MOBILIN/CLM
L26      493 (SULINDAC/CLM OR CLINORIL/CLM OR AFLODAC/CLM OR MOBILIN/(

=> s l26 and l25
L27        13 L26 AND L25

=> s cancer? or tumor? or neoplas?
      78408 CANCER?
      65529 TUMOR?
      22767 NEOPLAS?
L28   97667 CANCER? OR TUMOR? OR NEOPLAS?

=> s l27 and l28
L29        12 L27 AND L28

=> s l18/clm
L30     2678 (SYNERG?/CLM)

=> s l30 and l29
L31        11 L30 AND L29

=> s l31 not py>2003
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     291160 PY>2003
L32        10 L31 NOT PY>2003

=> d ibib 1-5

L32   ANSWER 1 OF 10   PCTFULL  COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:      2003030821 PCTFULL  ED 20030428  EW 200316
TITLE (ENGLISH):       ALBUMIN FUSION FPROTEINS
TITLE (FRENCH):        PROTEINES DE FUSION D'ALBUMINE
INVENTOR(S):           ROSEN, Craig, A., 22400 Rolling Hill Lane,
                       Laytonsville, MD 20882, US [US, US];
                       HASELTINE, William, A., 3053 P Street, N.W.,
                       Washington, DC 20007, US [US, US]
PATENT ASSIGNEE(S):    HUMAN GENOME SCIENCES, INC., 9410 Key West Aven
                       Rockville, MD 20850, US [US, US], for all designates
                       States except US;
                       ROSEN, Craig, A., 22400 Rolling Hill Lane,
                       Laytonsville, MD 20882, US [US, US], for US only;
                       HASELTINE, William, A., 3053 P Street, N.W.,
                       Washington, DC 20007, US [US, US], for US only
AGENT:                 WALES, Michele, M.$, Human Genome Sciences, Inc., 9410
                       Key West Avenue, Rockville, MD 20850$, US
LANGUAGE OF FILING:    English
LANGUAGE OF PUBL.:     English
DOCUMENT TYPE:         Patent
PATENT INFORMATION:
                       NUMBER          KIND    DATE
                       --------------------------------
                       WO 2003030821       A2 20030417
DESIGNATED STATES
    W:                  AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
                       CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
                       IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
                       MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
                       SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
    RW (ARIPO):     GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
    RW (EAPO):      AM AZ BY KG KZ MD RU TJ TM
    RW (EPO):       AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC
                       NL PT SE SK TR
    RW (OAPI):      BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.:     WO 2002-US31794      A  20021004
PRIORITY INFO.:        US 2001-60/327,281      20011005

L32   ANSWER 2 OF 10   PCTFULL  COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:      2002077186 PCTFULL  ED 20021011  EW 200240
TITLE (ENGLISH):       HUMAN SECRETED PROTEINS
TITLE (FRENCH):        PROTEINES SECRETEES PAR L'ETRE HUMAIN
INVENTOR(S):           ROSEN, Craig, A., 2240 Rolling Hill Lane, Laytonsville,
                       MD 20882, US [US, US];
                       RUBEN, Steven, M., 18528 Heritage Hills Drive, Olney,
                       MD 20832, US [US, US]
PATENT ASSIGNEE(S):    HUMAN GENOME SCIENCES, INC., 9410 Key West Aven
                       Rockville, MD 20850, US [US, US], for all designates
                       States except US;
                       ROSEN, Craig, A., 2240 Rolling Hill Lane, Laytonsville,
                       MD 20882, US [US, US], for US only;
                       RUBEN, Steven, M., 18528 Heritage Hills Drive, Olney,
                       MD 20832, US [US, US], for US only
AGENT:                 HOOVER, Kenley, K.$, Human Genome Sciences, Inc., 9410
                       Key West Avenue, Rockville, MD 20850$, US
LANGUAGE OF FILING:    English
LANGUAGE OF PUBL.:     English
DOCUMENT TYPE:         Patent
PATENT INFORMATION:
                       NUMBER          KIND    DATE
                       --------------------------------
                       WO 2002077186       A2 20021003
DESIGNATED STATES
    W:                  AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
                       CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
                       IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
                       MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL
                       TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
    RW (ARIPO):     GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
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RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2002-US9188 A 20020326
PRIORITY INFO.: US 2001-60/278,650 20010327
US 2001-09/950,082 20010912
US 2001-09/950,083 20010912

L32 ANSWER 3 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2002072763 PCTFULL ED 20020927 EW 200238
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): SHI, Yanggu, 437 West Side Drive, Apt. 102, Gaithersburg, MD 20878, US [US, US];
NI, Jian, 17815 Fair Lady Way, Germantown, MD 20874, US [CN, US];
RUBEN, Steven, M., 18528 Heritage Hills Drive, Olney, MD 20832, US [US, US]
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC., 9410 Key West Aven Rockville, MD 20850, US [US, US], for all designates States except US;
SHI, Yanggu, 437 West Side Drive, Apt. 102, Gaithersburg, MD 20878, US [US, US], for US only;
NI, Jian, 17815 Fair Lady Way, Germantown, MD 20874, US [CN, US], for US only;
RUBEN, Steven, M., 18528 Heritage Hills Drive, Olney, MD 20832, US [US, US], for US only
AGENT: HOOVER, Kenley, K.$, Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002072763	A2	20020919

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2002-US6990 A 20020308
PRIORITY INFO.: US 2001-60/274,214 20010309

L32 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055368 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055368	A1	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY

DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US1348 A 20010117

PRIORITY INFO.:

US 2000-60/179,065	20000131
US 2000-60/180,628	20000204
US 2000-60/184,664	20000224
US 2000-60/186,350	20000302
US 2000-60/189,874	20000316
US 2000-60/190,076	20000317
US 2000-60/198,123	20000418
US 2000-60/205,515	20000519
US 2000-60/209,467	20000607
US 2000-60/214,886	20000628
US 2000-60/215,135	20000630
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US 2000-60/231,413	20000908
US 2000-60/232,080	20000908
US 2000-60/231,414	20000908
US 2000-60/231,244	20000908
US 2000-60/232,081	20000908
US 2000-60/231,242	20000908
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US 2000-60/235,836	20000927
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US 2000-60/236,327	20000929
US 2000-60/236,370	20000929
US 2000-60/236,368	20000929

US 2000-60/236,367 20000929
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US 2000-60/237,038 20001002
US 2000-60/237,040 20001002
US 2000-60/237,037 20001002
US 2000-60/236,802 20001002
US 2000-60/239,937 20001013
US 2000-60/239,935 20001013
US 2000-60/241,785 20001020
US 2000-60/241,809 20001020
US 2000-60/240,960 20001020
US 2000-60/241,787 20001020
US 2000-60/241,808 20001020
US 2000-60/241,221 20001020
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L32 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055328 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;

ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055328	A2	20010802

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US1359 A 20010117

PRIORITY INFO.:

US 2000-60/179,065	20000131
US 2000-60/180,628	20000204
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

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L32 ANSWER 6 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055205 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055205	A1	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2001-US1337 A 20010117
PRIORITY INFO.: US 2000-60/179,065 20000131
US 2000-60/180,628 20000204
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US 2000-60/251,990 20001208
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L32 ANSWER 7 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055203 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055203	A1	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2001-US1327 A 20010117
PRIORITY INFO.: US 2000-60/179,065 20000131
US 2000-60/180,628 20000204
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US 2001-60/259,678 20010105

L32 ANSWER 8 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055201 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055201	A1	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
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TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2001-US1317 A 20010117
PRIORITY INFO.: US 2000-60/179,065 20000131
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L32 ANSWER 9 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055164 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055164	A1	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN

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MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
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SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
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APPLICATION INFO.: WO 2001-US1566 A 20010117
PRIORITY INFO.: US 2000-60/179,065 20000131
US 2000-60/180,628 20000204
US 2000-60/184,664 20000224
US 2000-60/189,874 20000316
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US 2000-60/251,989 20001208

L32 ANSWER 10 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001054733 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:
NUMBER KIND DATE

WO 2001054733 A1 20010802
DESIGNATED STATES
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APPLICATION INFO.: WO 2001-US1312 A 20010117
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

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L32 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN

CLM data too large for display

=> d kwic 1

L32 ANSWER 1 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		17.38	57.47

STN INTERNATIONAL LOGOFF AT 15:04:59 ON 23 MAY 2006